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14. ABSTRACT

Our first two-year period of funding focused on using the meta-analytic approach to examine the effects of exercise on BMD in adult humans using summary means from completed studies. Since no meta-analysis had existed using individual patient data (IPD) to examine the effects of exercise on BMD, our second two-year period of funding was devoted to examining the feasibility of such. The major conclusions from this work are as follows: (1) site-specific, weight bearing exercise appears to increase and/or maintain BMD anywhere from 1% to 3% in both men and women, (2) when conducting meta-analytic research, either the original metric or standardized effect size can be used when analyzing data dealing with the effects of exercise on BMD in adults, (3) Given the poor response rate in the retrieval of IPD, the use of summary means meta-analyses may be more appropriate for studies dealing with the effects of exercise on BMD in adults, (4) Adherence to the recent recommendations from the American College of Sports Medicine regarding physical activity and bone health should bring about the 1% to 3% benefit observed in our meta-analytic work.

15. SUBJECT TERMS
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I. INTRODUCTION

Bone health is critical for optimal performance and the prevention of fractures associated with low bone mineral density (BMD). Our first two-year period of funding focused on using the meta-analytic approach to examine the effects of exercise on BMD in adult humans using summary means from completed studies. Since no meta-analysis had existed using individual patient data (IPD) to examine the effects of exercise on BMD, our second two-year period of funding was devoted to examining the feasibility of such. The funding period to complete this project was extended, at no additional cost, for several years because of the Principal Investigator's two moves to different universities for the purpose of enhancing his research program.

II. BODY

A. Statement of Work – As can be seen in the table below, all approved work has been accomplished.

1. Summary Means Meta-Analyses

Task	Task Accomplished?
Conduct literature search	Yes
- computer	Yes
- hand	Yes
- contact experts to review references	Yes
Copy, classify, relevant studies	Yes
Develop, refine, modify coding sheet	Yes
Contact experts to review coding sheets	Yes
Begin coding of studies	Yes
Final coding of studies	Yes
Analysis of compiled data	Yes
- Main effects	Yes
- Interactions	Yes
- Inferential	Yes
Evaluate results	Yes
Prepare & present data at conferences	Yes
Prepare & publish manuscripts and reports	Yes

2. Individual Patient-Data Meta-Analyses

Task	Task Accomplished?
1. Search for addresses of authors to request data from	Yes
2. Prepare and validate forms	Yes
- Cover letter	Yes
- Data request forms	Yes
3. Mail data request forms to authors	Yes
- Initial mailing	Yes
- Follow-up mailing	Yes
4. Coding	Yes

- Modify coding sheet to handle individual patient data	Yes
- Enter data retrieved	Yes
5. Analyze data	Yes
6. Prepare and present results at conferences	Yes
7. Prepare and publish manuscripts	Yes

B. Study-Specific Summary of Completed Research

We have learned much from the four years of funding that we received for this project. As a result of this important support, we have published seven manuscripts in peer-reviewed biomedical journals (Appendix D)[3-9] as well as seven abstracts (Appendix E). Most notably and to the best of our knowledge, we are the **first** research group to examine the effects of exercise on an outcome, in this case changes in BMD, using the IPD meta-analysis approach and the **first** group to publish a methods paper on the retrieval of IPD in any field. For ease of understanding and interpretation, we have divided this section into (1) the effects of exercise on BMD outcomes in men, (2) the effects of exercise on BMD outcomes in women, and (3) methodological findings in relation to conducting meta-analytic work dealing with the effects of exercise on BMD in adults.

1. Exercise and BMD in men. Osteoporosis and low bone mass are major public health problems among men, affecting more than 5,000,000 individuals 50 years of age and older in the United States.[11] Exercise, a low-cost nonpharmacologic intervention that is available to the vast majority of males, may help to improve and/or maintain BMD.[10] Using the summary means meta-analytic approach, we examined the effects of exercise on BMD in men.[5] A total of 26 effect sizes (ES) representing 225 subjects from only 8 studies met the criteria for inclusion. When BMD sites assessed were specific to the sites loaded during exercise, increases of 2.6% (2.1% in the exercisers and -0.5% in the controls) were found. These results were statistically significant (ES = 0.213, 95% bootstrap confidence interval = 0.007–0.452). Statistically significant ES changes were found for older (>31 years of age) but not younger (≤31 years of age) adults, with differences between groups statistically significant ($p = 0.04$). Statistically significant site-specific changes were also observed at the femur, lumbar, and os calcis sites. The results of this study suggest that site-specific exercise may help improve and maintain BMD at the femur, lumbar, and os calcis sites in older men. However, the biological importance of the small changes observed for most outcomes is not known. In addition, a need exists for additional studies dealing with the effects of exercise on BMD in men.

2. Exercise and BMD in women. Osteopenia and osteoporosis are major public health problems in the United States, affecting primarily lean, white, postmenopausal women. Currently more than 26 million white, postmenopausal women in the United States have either osteopenia or osteoporosis with these numbers expected to increase as a result of an increase in the number of older adults. [11] Similar to recommendations for men, exercise has been advocated for helping to improve and/or maintain BMD in women. [10] Using both the summary means and IPD meta-analytic approaches, we have published five studies dealing with the effects of exercise on BMD in women.[3;4;6;7;9]

Using the summary means meta-analytic approach, we examined the effects of progressive resistance training on BMD at the femur, lumbar spine, and radius in pre- and postmenopausal women.[6] Twenty-nine studies representing 94 ES (femur = 53, lumbar spine = 24, radius = 17) from 61 groups (32 exercise, 29 control) were included. Across all categories, resistance training had a positive effect on BMD at the lumbar spine of all women ($p < 0.05$). These changes were equivalent to a relative benefit of 1.26% in the exercise groups (0.19% decrease in the exercise groups and a 1.45% decrease in the control groups). When limited to postmenopausal women, statistically significant improvements ($p < 0.05$) were found at the femur and radius sites. Changes in BMD at the femur were equivalent to a relative benefit of 0.61% (0.40% increase in the exercise groups and a 0.21% decrease in the controls) while changes at the radius were equivalent to a benefit of 2.69% (0.82% increase in BMD in the exercise groups and a 1.87% decrease in the control groups). It was concluded that resistance training has a beneficial effect on BMD in women.

A second study we published used the IPD meta-analysis approach to examine the efficacy of resistance exercise on lumbar spine and femoral neck BMD in premenopausal women.[9] One hundred forty-three subjects (74 exercise, 69 control) were included in the analysis. Changes in lumbar spine BMD averaged 0.006 ± 0.035 g/cm^2 ($0.64 \pm 2.99\%$) in the exercise group and 0.008 ± 0.091 g/cm^2 ($0.74 \pm 7.58\%$) in the control group while changes in femoral neck BMD averaged 0.005 ± 0.031 g/cm^2 ($0.46 \pm 3.10\%$) in the exercise group and 0.003 ± 0.031 g/cm^2 ($0.31 \pm 2.97\%$) in the control group. No statistically significant differences in lumbar spine or femoral neck BMD were found within or between the exercise and control groups ($p > 0.05$). We concluded that our results do not support the efficacy of resistance exercise for increasing or maintaining lumbar spine and femoral neck BMD in premenopausal women. These findings are similar to our previous findings at the femur but not the lumbar spine in premenopausal women. [6] One of the reasons for these discrepant results may have to do with the fact that the studies included in our IPD meta-analysis did not adequately load the lumbar spine. A second possible reason may be because optimal BMD is usually present during the premenopausal years. A third possible reason for the lack of statistically significant findings may have to do with the fact that we were only able to obtain IPD from approximately 25% of the eligible studies. Given the problems with this IPD meta-analysis, we believe that our previous summary means meta-analysis better reflects the true effects of progressive resistance training on BMD in women. [6]

Another study we published used the summary means meta-analytic approach to examine the effects of aerobic exercise on regional BMD (lumbar spine, femur, and radius) in pre- and postmenopausal women.[3] Twenty-four studies representing 54 groups (31 exercise, 27 control) and 1029 subjects (517 exercise, 512 control) met the criteria for inclusion. Using a random-effects model, small but statistically significant effect size changes in BMD were observed at the lumbar spine and femur ($p < 0.05$). Changes in lumbar spine BMD were equivalent to an overall relative benefit of 2.24% in the exercise group (0.37% increase in the exercise groups and 1.87% decrease in the

control groups) while changes at the femur were equivalent to a 1.95% benefit (1.37% increase in the exercise groups and a .0.58% decrease in the control groups). No statistically significant changes were observed at the radius ($p > 0.05$). We concluded that aerobic exercise has a small but positive effect on BMD at the lumbar spine and femur in women.

We published a fourth study that used the IPD meta-analysis approach to examine the effects of exercise (aerobic and progressive resistance exercise) on lumbar spine BMD in postmenopausal women.[7] Thirteen trials that included 699 subjects (355 exercise, 344 controls) were included in the analysis. Across all categories, a statistically significant benefit of approximately 2% was found at the lumbar spine ($p < 0.05$). Changes were equivalent to an approximate 1% increase in the exercise group and a 1% decrease in the control group. We concluded that exercise helps to improve and maintain lumbar spine BMD in postmenopausal women.

In a similar study to the one previously described, we used the IPD meta-analysis approach to examine the effects of aerobic and progressive resistance training on femoral neck BMD in postmenopausal women.[4] Ten controlled clinical trials that included 595 subjects (aged 42-92 years) met our criteria for inclusion. Across all designs and categories, there was a nonsignificant ($p > 0.05$) benefit of 0.28% in femoral neck BMD for the exercise group (0.73% increase in the exercise group and 0.45% increase in the control group). We concluded that the exercise protocols used in this IPD meta-analysis did not improve femoral neck BMD in postmenopausal women. Our findings are in conflict with our previous meta-analytic work in which an approximate 2% improvement in BMD was found at the hip as a result of site-specific aerobic exercise and progressive resistance training.[1;6] One of the possible reasons for the discrepant results between studies may have to do with the fact that the summary measures that were obtained in our previous research were the result of pooling the outcomes from all sites that were assessed at the femur (femoral neck, Ward's triangle, trochanter, intertrochanter) because of the small sample sizes available. Consequently, it may be that improvements in BMD occur at sites other than the femoral neck (Ward's triangle, trochanter, intertrochanter).

3. Methods studies. We have published two methods studies using summary means meta-analysis and IPD meta-analysis.[2;8] One study compared the use of the common metric versus standardized difference effect size for pooling results from a sample of controlled trials examining the effects of exercise on BMD at the hip in postmenopausal women.[2] The most commonly reported metric (percent change) was compared to the standardized difference effect size. A total of 13 values were included in the analysis. Using a fixed-effects model, the common metric (CM+) effect size showed an increase of 0.36 percent (95 percent confidence interval = -0.09 to 0.81). From a clinical perspective, this would be considered a "small" effect. The standardized approach (STD+) showed an average effect of 0.20 (95 percent confidence interval = 0.02 to 0.38). This would also be considered a "small" effect. No significant heterogeneity (Q) was observed for either common metric or standardized results (common metric, $Q = 18.80$, $p = 0.09$, standardized difference, $Q = 13.61$, $p = 0.33$). It was concluded that

for this set of studies, the use of either the most commonly reported metric (percent change) or the standardized effect size produced similar results. This evidence supports using the commonly reported metric when studies included in a meta-analysis report outcomes in the same metric. For clinicians and researchers, use of the common metric will be more clinically meaningful and will enhance interpretation of results for a wider range of readers.

A second methods paper examined the feasibility of acquiring IPD for a meta-analysis on the effects of exercise on BMD in adults.[8] We were able to obtain data from 29 (38.2%) of the 76 eligible studies. Binary multiple logistic regression analysis revealed a trend suggesting that authors of studies conducted in the United States were less likely to supply IPD when compared with authors who conducted studies in other countries (adjusted odds ratio, 0.324; 95% confidence interval, 0.104-1.004). Only 19% of authors from studies conducted in the United States vs. 52.9% of authors from other countries were willing to provide us with IPD despite the fact that they were financially compensated for such. We concluded that we received a low response rate in the acquisition of IPD for a meta-analysis dealing with the effects of exercise on BMD in adults. The use of summary means vs. IPD may be more appropriate for studies of this nature.

III. KEY RESEARCH ACCOMPLISHMENTS FOR PROJECT PERIOD

A. Developed reference database of intervention studies dealing with the effects of exercise on BMD in adults (Appendix A).
B. Developed code book (Appendix B) and coded summary means data for all eligible intervention studies dealing with the effects of exercise on BMD in adults.
C. Developed code book (Appendix C) and coded IPD for all eligible intervention studies dealing with the effects of exercise on BMD in adults.
D. Published, in peer-reviewed biomedical journals, six summary means and IPD meta-analysis papers as well as one methods paper dealing with the effects exercise on BMD in adults (Appendix D).
E. Published seven abstracts, including two methods studies, dealing with the effects of exercise intervention studies on BMD in adults (Appendix E).

IV. REPORTABLE OUTCOMES FOR PROJECT PERIOD

A. Articles Published (Appendix D)

1. **Kelley, G.A.,** Kelley, K.S., Tran, Z.V. (2000). Exercise and bone mineral density in men: A meta-analysis. Journal of Applied Physiology. 88:1730-1736.

2. **Kelley, G.A.**, Kelley, K.S., Tran, Z.V. (2001). Resistance training and bone mineral density in women: A meta-analysis of controlled trials. American Journal of Physical Medicine and Rehabilitation. 80:65-77.

3. **Kelley, G.A**., Kelley, K.S., Tran, Z.V. (2002). Retrieval of individual patient data for an exercise-related meta-analysis. American Journal of Medicine & Sports. 4:350-354.

4. **Kelley, G.A.**, Kelley, K.S., Tran, Z.V. (2002). Aerobic exercise and regional bone density in women: A meta-analysis of controlled trials. American Journal of Medicine & Sports. 4:427-433, 452.

5. **Kelley, G.A**., Kelley, K.S., Tran, Z.V. (2002). Exercise and lumbar spine bone mineral density in postmenopausal women: A meta-analysis of individual patient data. Journal of Gerontology: Medical Sciences. 57:M599-M604.

6. **Kelley, G.A,** Kelley, K.S., Tran ZV. (2004). Efficacy of resistance exercise on lumbar spine and femoral neck bone mineral density in premenopausal women: A meta-analysis of individual patient data. Journal of Women's Health. 13:293-300.

7. **Kelley, G.A,** Kelley K.S. (2006). Exercise and bone mineral density at the femoral neck in postmenopausal women: A meta-analysis of controlled clinical trials using individual patient data. American Journal of Obstetrics and Gynecology. 194:760-767.

B. Abstracts Published (Appendix E)

1. **Kelley, G.A.,** Kelley, K.S. (1999). Common metric versus standardized difference for meta-analysis of bone density studies. Medicine and Science in Sports and Exercise. 31 (Suppl 5):S249.

2. **Kelley, G.A.,** Kelley, K.S. (2000). Resistance training and bone mineral density in women: A meta-analysis of controlled trials. Research Quarterly for Exercise and Sport. 71 (Suppl 1):A29.

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5. **Kelley, G.A**., Kelley, K.S. (2002) Exercise and lumbar spine bone mineral density in postmenopausal women: A meta-analysis of individual patient data. American Public Health Association Access at: http://www.apha.org/meetings/future_past.htm

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7. **Kelley, G.A.,** Kelley, K.S. (2005). Exercise and bone mineral density at the femoral neck in postmenopausal women: A meta-analysis of controlled clinical trials using

individual patient data. American Public Health Association Access at: http://apha.confex.com/apha/133am/techprogram/paper_110770.htm

B. Personnel (Paid)

1. Dr. George A. Kelley, FACSM – Principal Investigator
2. Kristi Sharpe-Kelley, M.Ed. – Research Technician
3. Dr. Christine Snow-Harter – Consultant
4. Dr. Charlotte Sanborn - Consultant

V. CONCLUSIONS FOR PROJECT PERIOD

A. Implications of Completed Research

The overall results of our research lead us to the following major conclusions:

1. Site-specific, weight bearing exercise appears to increase and/or maintain BMD anywhere from 1% to 3% in both men and women.
2. When conducting meta-analytic research, either the original metric or standardized effect size can be used when analyzing data dealing with the effects of exercise on BMD in adults.
3. Given the poor response rate in the retrieval of IPD, the use of summary means meta-analyses may be more appropriate for studies dealing with the effects of exercise on BMD in adults.
4. Adherence to the recent recommendations for physical activity and bone health should bring about the 1% to 3% benefit observed in our meta-analytic work. [10] These training recommendations are as follows:

Variable	Recommendation
Mode:	weight-bearing endurance activities (tennis; stair climbing; jogging, at least intermittently during walking), activities that involve jumping (volleyball, basketball), and resistance exercise (weight lifting)
Intensity:	moderate to high, in terms of bone-loading forces
Frequency:	weight-bearing endurance activities 3–5 times per week; resistance exercise 2–3 times per week
Duration:	30–60 minutes per day of a combination of weight-bearing endurance activities, activities that involve jumping, and resistance exercise that targets all major muscle groups

B. Suggestions for Future Research

Despite the fact that studies can be more objectively evaluated using the meta-analytic versus traditional, narrative approach, potential problems still exist. In general, the very nature of meta-analysis dictates that the meta-analysis itself inherits those limitations that exist in the literature. Therefore, it is the responsibility of the meta-analyst to point out these limitations and provide directions for future research. For example, we would suggest that future studies dealing with the effects of exercise on BMD do a better job

of assessing and reporting on the dietary habits of their subjects as well as the types of pharmacologic interventions that subjects may be taking. Furthermore, since few studies included an assessment of the alcohol and calcium intake of subjects, greater attention to these factors in the future appear warranted. In addition, an assessment of the impact of selected exercises on bone (for example, ground reaction forces in running) is needed. Consequently, more precise exercise guidelines for enhancing BMD will be possible. It is also recommended that future studies include an evaluation of their data using both an analysis-by-protocol as well as an intention-to-treat approach. As a result, one may examine both the efficacy and effectiveness of exercise for enhancing BMD in adults. This will help provide clinicians with more meaningful information regarding the use of exercise for enhancing BMD.

Since the assessment of BMD at the hip most commonly included the femoral neck, it is suggested that additional studies also include other sites at the femur (trochanter, intertrochanteric, Ward's triangle) so that one can determine the true effects of exercise on BMD at these sites. In addition, since most progressive resistance training studies relied predominantly on upper versus lower body exercises in their protocols, it would appear plausible to suggest that future studies that use progressive resistance training as an intervention include additional lower leg exercises when examining changes in BMD at the femur. Furthermore, given the paucity of studies in men, additional studies in this population group are needed. Finally, it would appear plausible to suggest that a need exists for large randomized trials that examine the effects of exercise on BOTH BMD and fracture risk. It would be especially interesting to examine whether the benefits in BMD observed in our meta-analytic work (1% to 3%) result in clinically meaningful reductions in fracture risk. From a military perspective, an examination of the effects on exercise on BMD in adolescents may be especially important given the average age of enlistees.

We had a low response rate in the acquisition of IPD for our meta-analyses dealing with the effects of exercise training on BMD in adult humans, especially when requesting IPD from studies conducted in the United States. However, since we cannot generalize as to the success of obtaining IPD from other pharmacologic and nonpharmacologic interventions, it would appear plausible to suggest that an examination of the ability to retrieve IPD for other interventions is warranted. One of the possible reasons for the low response rate, especially from studies conducted in the United States, may have to do with the investigators' concerns about protecting their data because of the potential misuse of such. For example, the strict guidelines that are enforced by the vast majority of university and hospital institutional review boards in the United States surrounding issues such as subject confidentiality may have precluded authors from supplying us with IPD. However, we believe that concerns about approbation from institutional review boards should not be an issue, as researchers should have data storage systems that protect the confidentiality of patients. Consequently, the sharing of IPD should not be a problem. Researchers who stated that the data are "no longer available" were troubling in that the failure to sustain IPD in a manner that allows for verification of an analysis might be considered an ethical issue. Alternatively, this may be an issue of nothing more than selfishness on the part of some investigators. Since cooperation and

trust are part of the foundation of science, we believe that any acts of selfishness on the part of investigators should be discouraged and that investigators should be willing to supply others with their IPD when requested. Unfortunately, since we don't anticipate any rapid changes in these behaviors, it is recommended that future meta-analytic research examining the effects of exercise on BMD focus on using summary means rather than IPD.

C. So What?

Osteoporosis and osteopenia are major public health problems among both men and women. The results of our research suggest that site-specific exercise can benefit BMD anywhere from 1% to 3%. These benefits may reduce the risk for subsequent fracture.

VI. REFERENCES

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VII. APPENDICES

A. Reference List of BMD Studies
B. Codebook for Summary Means Meta-Analyses
C. Codebook for IPD Meta-Analyses
D. Publications in Peer-Reviewed Biomedical Journals
E. Published Abstracts of Presentations at Professional Conferences

APPENDIX A
Reference List of BMD Studies

EXERCISE AND BONE MINERAL DENSITY REFERENCES

These references below are limited to those that met the following inclusion criteria: (1) randomized and non-randomized clinical trials dealing with the effects of aerobic and/or resistance exercise in humans, (2) non-exercise control group or control period included, (3) studies in the English-language literature (journal articles, dissertations, masters theses) published and indexed between January 1962 and December 1998, (4) changes in bone mineral density (regional, total) reported in adults ages 18 years and older.

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APPENDIX B
Codebook for Summary Means Meta-Analyses

C#	VARIABLE	DESCRIPTION
1	Row #	Row number
2	ID#	Study id number
3	Author	Author(s) of study
4	Group-Described	Description of group/effect size
5	SC	Will this row be used to analyze data according to study characteristics? Coded as Yes or No
6	GC-Ex	Will this row be used to analyze data according to exercise group characteristics? Coded as Yes or No
7	GC-Con	Will this row be used to analyze data according to control group characteristics? Coded as Yes or No
8	Source	Coded as journal, dissertation or other
9	Year	Year study was published
10	Language	Language of journal
11	Country	Country study was conducted in
12	Design	Study design, coded as randomized control trial (RCT) or controlled trial (CT)
13	Matching	matching procedures, coded as age (age), height (ht), weight (wt), body mass index (BMI), max vo2 (VO2max), yrs. postmenopauase (yrspm)
14	Crossover trial	Was the study a crossover trial? Coded as yes or no
15	Study Quality	rating of study quality score will be generated from quality rating scale of Jadad et al.
16	Analysis?	Analysis: coded as intention to treat (ITT) or analysis by protocol (ABP) or analysis by protocol with follow-up (ABPWF)
17	#Groups-Ex	number of exercise groups
18	#Groups-Con	number of control groups
19	#Groups-Total	total number of groups (automatically calculated)
20	#ES-Total	total number of effect sizes
21	InitialN-Ex	initial number of exercise subjects
22	InitialN-Con	initial number of control subjects
23	InitialN-Total	initial total number of subjects (automatically calculated)
24	FinalN-Ex	final number of exercising subjects
25	FinalN-Con	final number of control subjects
26	FinalN-Total	final total number of subjects (automatically calculated)
27	%Dropout-Ex	percent dropout in the exercise groups (automatically calculated)
28	%Dropout-Con	percent dropout in the control groups (automatically calculated)
29	%-Females	% of female subjects in the study
30	Race	Ethnicity of subjects
31	Total N-Ex+Co	Total number of subjects bone density was assessed in (exercise plus control) (automatically calculated)
32	BONE RESULTS	leave as is
33	N-Ex	Number of exercising subjects
34	I-Ex	initial bone density for exercise groups
35	I-SD-Ex	standard deviation for bone density of the exercise groups
36	F-Ex	final bone density for the exercise groups
37	F-SD-Ex	standard deviation for final bone density for the exercise groups
38	D-Ex	difference in bone density for the exercise groups (automatically calculated)
39	D-SD-Ex	standard deviation of the difference in bone density for exercise groups
40	P-Ex	% change in bone density for the exercise groups (automatically calculated)
41	P-SD-Ex	standard deviation of difference in % change in bone density for exercise groups
42	N-Con	Number of subjects in the control groups
43	I-Con	initial bone density for the control groups
44	I-SD-Con	initial standard deviation for bone density in the control groups

C#	VARIABLE	DESCRIPTION
45	F-Con	final bone density for the control groups
46	F-SD-Con	final standard deviation for bone density in the control groups
47	D-Con	difference in bone density for the control groups (automatically calculated)
48	D-SD-Con	standard deviation of the difference in bone density for the control groups
49	P-Con	% change in bone density for the control groups (automatically calculated)
50	P-SD-Con	standard deviation for % change in bone density for the control groups
51	P-Ex-Con	percent change for exercise and control groups (automatically calculated)
52	Metric	Metric used for bone density. Code as reported (ex . gm/cm 3)
53	ES-Method	method used for calculating bone density effect size, coded as pre-post, or change outcome, other
54	ES-Raw(g)	raw effect size (g) calculated from DSTAT program (calculate later)
55	ES-Corrected(d)	effect size(d) corrected for small sample bias (automatically calculated later)
56	ES-Var(d)	effect size variance (automatically calculated later)
57	ES-SD(d)	effect size (SD) for bone density (automatically calculated later)
58	ES-L95CI(d)	lower 95%CI for effect size (automatically calculated later)
59	ES-U95CI(d)	upper 95%CI for effect size (automatically calculated)
60	Significant?	Did the author(s) report the results to be statistically significant in favor of the treatment group? coded as yes or no.
61	PHYSICAL TRAITS	leave as is
62	Age-Ex	age of exercise groups
63	Age-SD-Ex	standard deviation for age of exercise groups
64	Age Range-Ex	age range for exercise groups
65	Height-Ex	height (cm) for exercise groups
66	Height-SD-Ex	standard deviation for height of exercise groups
67	I-Weight-Ex	initial weight (kg) for exercise groups
68	I-Weight-SD-Ex	standard deviation for initial weight (kg) of exercise groups
69	F-Weight-Ex	final weight (kg) for exercise groups
70	F-Weight-SD	standard deviation for final weight (kg) for exercise groups
71	D-Weight-Ex	difference in weight (kg) for exercise groups (automatically calculated)
72	D-Weight-SD-Ex	standard deviation for the difference in weight (kg) for exercise groups (automatically calculated)
73	P-Weight-Ex	% change in weight (kg) for the exercise groups (automatically calculated)
74	I-BMI-Ex	initial body mass index for the exercise groups
75	I-BMI-SD-Ex	standard deviation for initial body mass index for the exercise groups
76	F-BMI-Ex	final body mass index for the exercise groups
77	F-BMI-SD-Ex	standard deviation for initial body mass index for the exercise groups
78	D-BMI-Ex	difference in body mass index for the exercise groups (automatically calculated)
79	D-BMI-SD-EX	standard deviation of the difference in body mass index for the exercise groups (automatically calculated)
80	P-BMI-Ex	% change in body mass index for the exercise groups (automatically calculated)
81	I-Fat-Ex	initial % fat for exercise groups
82	I-Fat-SD-Ex	standard deviation for initial % fat for exercise groups
83	F-Fat-Ex	final % fat for exercise groups
84	F-Fat-SD-Ex	standard deviation for final % fat for exercise groups
85	D-Fat-Ex	difference in % fat for exercise groups (automatically calculated)
86	D-Fat-SD-Ex	standard deviation for difference in % fat (automatically calculated)
87	P-Fat-Ex	% fat for exercise groups (automatically calculated)
88	I-LBM-Ex	initial lean body mass (kg) for exercise groups

C#	VARIABLE	DESCRIPTION
89	I-LBM-SD-Ex	standard deviation for initial lean body mass (kg)for exercise groups
90	F-LBM-Ex	final lean body mass (kg) for exercise groups
91	F-LBM-SD-Ex	standard deviation for final lean body mass (kg) for exercise groups
92	D-LBM-Ex	difference in lean body mass (kg) for exercise groups (automatically calculated)
93	D-LBM-SD-Ex	standard deviation of the difference in lean body mass (kg) for exercise groups (automatically calculated)
94	P-LBM-Ex	% change in lean body mass (kg) for exercise groups (automatically calculated)
95	I-VO2-Ex	initial maximum oxygen consumption (ml/kg/min) for exercise groups
96	I-VO2-SD-Ex	standard deviation for initial maximum oxygen consumption (ml/kg/min) for exercise groups
97	F-VO2-Ex	final maximum oxygen consumption (ml/kg/min) for exercise groups
98	F-VO2-SD-Ex	standard deviation for maximum oxygen consumption (ml/kg/min) for exercise groups
99	D-VO2-Ex	difference in maximum oxygen consumption (ml/kg/min) for exercise groups (automatically calculated)
100	D-VO2-SD-Ex	difference in maximum oxygen consumption (SD in ml/kg/min) for exercise groups (automatically calculated)
101	P-VO2-Ex	% change in maximum oxygen consumption (ml/kg/min) for exercise groups (automatically calculated)
102	I-RHR-Ex	initial resting heart rate (bts/min) for the exercise groups
103	I-RHR-SD-Ex	standard deviation for initial resting heart rate (bts/min) for exercise groups
104	F-RHR-Ex	final resting heart rate (bts/min) for exercise groups
105	F-RHR-SD-Ex	standard deviation for final resting heart rate (bts/min) for the exercise groups
106	D-RHR-Ex	difference in resting heart rate (bts/min) for the exercise groups (automatically calculated)
107	D-RHR-SD-Ex	standard deviation for the difference in resting heart rate (bts/min) for exercise groups (automatically calculated)
108	P-RHR-Ex	% change in resting heart rate (bts/min) for exercise groups (automatically calculated)
109	%D-Strength-Ex	percent change in strength for the exercise groups
110	Postmenopausal?-Ex	were subjects postmenopausal women: coded as yes, no, some
111	Yrs Postmenopause-Ex	number of years exercising subjects were postmenopausal
112	Yrs Postmenopause-SD-Ex	standard deviation for number of years exercising women were postmenopausal
113	I-Ca-Ex	initial calcium levels for exercise subjects
114	I-Ca-SD-Ex	initial standard deviation for calcium levels for exercise subjects
115	F-Ca-Ex	final calcium levels for exercise subjects
116	F-Ca-SD-Ex	final standard deviation for calcium levels of exercising subjects
117	D-Ca-Ex	difference in calcium levels for exercising subjects (automatically calculated)
118	D-Ca-SD-Ex	standard deviation for differences in calcium levels for exercising subjects (automatically calculated)
119	%D-Ca-Ex	percent difference in calcium levels for exercising subjects (automatically calculated)
120	Ca-Supp-Ex	calcium supplementation for exercise subjects: coded as yes, no, some
121	Drugs-Ex	were any of the exercisers taking drugs to enhance bone density: coded as yes, no, some
122	Smoking-Ex	smoking status of exercising subjects: coded as yes, no, some
123	Alcohol-Ex	did exercising subjects drink alcohol?: coded as yes, no, some
124	Diet-Ex	did exercising subjects nutrition intake vary between initial and final testing: coded as yes, no, some
125	Previous PA-Ex	were the subjects previously active?: coded as yes, no, some
126	Previous Fractures-EX	did exercising subjects have previous fractures?: coded as yes, no, some
127	Age-Con	age for control groups
128	Age-SD-Con	standard deviation for age of control groups
129	Age Range-Con	age range for control groups
130	Height-Con	height (cm) for control groups
131	Height-SD-Con	standard deviation for height (cm) in control groups
132	I-Weight-Con	initial weight (kg) for control groups

C#	VARIABLE	DESCRIPTION
133	I-Weight-SD-Con	standard deviation for initial weight (kg) for control groups
134	F-Weight-Con	final weight (kg) for control groups
135	F-Weight-SD-Con	standard deviation for final weight (kg) for control groups
136	D-Weight-Con	difference in weight (kg) for control groups
137	D-Weight-SD-Con	standard deviation for difference in weight (kg) for control groups
138	P-Weight-Con	% change in weight (kg) for control groups
139	TE-Weight	treatment effect for differences in bodyweight
140	TE-Weight-Var	overall variance for treatment effect weight
141	TE-Weight-SD	standard deviation for treatment effect weight
142	TE-Weight-PCHG	treatment effect percent change for weight
143	I-BMI-Con	initial body mass index for control groups
144	I-BMI-SD-Con	standard deviation for initial body mass index in control groups
145	F-BMI-Con	final body mass index for control groups
146	F-BMI-SD-Con	standard deviation for final body mass index in control groups
147	D-BMI-Con	difference in body mass index for control groups
148	D-BMI-SD-Con	standard deviation for final body mass index for control groups
149	P-BMI-Con	% change in body mass index for control groups
150	TE-BMI	treatment effect for BMI (automatically calculated)
151	TE-BMI-Var	overall variance for BMI treatment effect (automatically calculated)
152	TE-BMI-SD	standard deviation for BMI treatment effect (automatically calculated)
153	TE-BMI-PCHG	treatment effect percent change for BMI (automatically calculated)
154	I-Fat-Con	initial %fat for control groups
155	I-Fat-SD-Con	initial %fat standard deviation for control groups
156	F-Fat-Con	final %fat for control groups
157	F-Fat-SD-Con	final %fat standard deviation for control groups
158	D-Fat-Con	differences in %fat for control groups
159	D-Fat-SD-Con	differences in %fat standard deviation for control groups
160	P-Fat-Con	% change difference in %fat for control groups
161	TE-Fat	treatment effect for %fat (automatically calculated)
162	TE-Fat-Var	overall variance for treatment effect %fat (automatically calculated)
163	TE-Fat-SD	standard deviation for %fat treatment effect (automatically calculated)
164	TE-Fat-PCHG	treatment effect percent change for %fat (automatically calculated)
165	I-LBM-Con	initial lean body mass (kg) for control groups
166	I-LBM-SD-Con	standard deviation for initial lean body mass (kg) for control groups
167	F-LBM-Con	final lean body mass (kg) for control groups
168	F-LBM-SD-Con	standard deviation for final lean body mass (kg) for control groups
169	D-LBM-Con	difference in lean body mass (kg) for control groups (automatically calculated)
170	D-LBM-SD-Con	standard deviation for differences in lean body mass (kg) for control groups
171	P-LBM-Con	% fat differences for lean body mass (kg) control groups (automatically calculated)
172	TE-LBM	treatment effect for lean doy mass (kg) (automatically calculated)
173	TE-LBM-Var	overall variance for treatment effect lean body mass (kg) (automatically calculated)
174	TE-LBM-SD	standard deviation for lean body mass (kg) treatment effect (automatically calculated)
175	TE-LBM-PCHG	treatment effect percent change for lean body mass (kg) (automatically calculated)
176	I-VO2-Con	initial maximum oxygen consumption (ml/kg/min) for control groups

C#	VARIABLE	DESCRIPTION
177	I-VO2-SD-Con	standard deviation for initial maximum oxygen consumption (ml/kg/min) for control groups
178	F-VO2-Con	final maximum oxygen consumption (ml/kg/min) for control groups
179	F-VO2-SD-Con	standard deviation for final maximum oxygen consumption (ml/kg/min) for control groups
180	D-VO2-Con	difference in maximum oxygen consumption (ml/kg/min) for control groups
181	D-VO2-SD-Con	standard deviation for differences in maximum oxygen consumption (ml/kg/min) for control groups
182	P-VO2-Con	% change difference in maximum oxygen consumption (ml/kg/min) for control groups
183	TE-VO2	treatment effect for maximum oxygen consumption (automatically calculated)
184	TE-VO2-Var	overall variance for maximum oxygen consumption treatment effect (automatically calculated)
185	TE-VO2-SD	standard deviation for maximum oxygen consumption treatment effect (automatically calculated)
186	TE-VO2-PCHG	treatment effect percent change for maximum oxygen consumption (automatically calculated)
187	I-RHR-Con	initial resting heart rate (bts/min) for control groups
188	I-RHR-SD-Con	standard deviation for initial resting heart rate (bts/min) for control groups
189	F-RHR-Con	final resting heart rate (bts/min) for control groups
190	F-RHR-SD-Con	standard deviation for final resting heart rate (bts/min) for control groups
191	D-RHR-Con	difference in resting heart rate (bts/min) for control groups (automatically calculated)
192	D-RHR-SD-Con	standard deviation for differences in resting heart rate (bts/min) for control groups (automatically calculated)
193	P-RHR-Con	% change in resting heart rate (bts/min) for control groups (automatically calculated)
194	TE-RHR	treatment effect for changes in resting heart rate (automatically calculated)
195	TE-RHR-Var	treatment effect variance for resting heart rate (automatically calculated)
196	TE-RHR-SD	treatment effect (SD) for resting heart rate (automatically calculated)
197	TE-RHR-PCHG	treatment effect percent change for resting heart rate (automatically calculated)
198	%D-Strength-Con	percent change in strength for the control group
199	TE-Strength-Ex-Con	treatment effect for strength (automatically calculated)
200	Postmenopausal?-Con	were control subjects postmenopausal: coded as yes, no, some
201	Yrs Postmenopause-Con	number of years control subjects were postmenopausal
202	Yrs Postmenopause-SD-Con	standard deviation for number of years control subjects were postmenopausal
203	I-Ca-Con	initial calcium levels for control subjects
204	I-Ca-SD-Con	initial standard deviation for calcium levels for control subjects
205	F-Ca-Con	final calcium levels for control subjects
206	F-Ca-SD-Con	final standard deviation for calcium levels of control subjects
207	D-Ca-Con	difference in calcium levels for control subjects (automatically calculated)
208	D-Ca-SD-Con	standard deviation for differences in calcium levels for control subjects (automatically calculated)
209	%D-Ca-Con	percent difference in calcium levels for exercising subjects (automatically calculated)
210	TE-Calcium	treatment effect for calcium levels (automatically calculated)
211	TE-Calcium-Var	treatment effect variance for calcium levels (automatically calculated)
212	TE-Calcium-SD	treatment effect (SD) for calcium (automatically calculated)
213	TE-Calcium-PCHG	percent change treatment effect for calcium levels (automatically calculated)
214	Ca-Supp-Con	calcium supplementation for exercise subjects: coded as yes, no, some
215	Drugs-Con	were any of the controls taking drugs to enhance bone density: coded as yes, no, some
216	Smoking-Con	smoking status of control subjects: coded as yes, no, some
217	Alcohol-Con	did control subjects drink alcohol? coded as yes, no, some
218	Diet-Con	did the nutrition intake of subjects vary between initial and final testing? coded as yes, no, some
219	Previous PA-Con	were the subjects active prior to taking part in the study? coded as yes, no, some
220	Previous Fractures-Con	did control subjects have previous fractures?: coded as yes, no, some

C#	VARIABLE	DESCRIPTION
221	BONE ASSESSMENT	leave as is
222	Type	type of bone assessment instrument used: coded as DEXA, DPA, QCT, SPA, Other
223	Model Name	model name of bone assessment instrument used: coded as reported in the study
224	Model #	model number of instrument used: coded as reported in the study
225	Total or Regional?	Was total and/or regional bone density assessed: coded as total or regional
226	Site-General	general sites assessed: coded as total, hip, back, forearm, heel, other
227	Site-Specific	specific sites assessed: coded as reported (for example L1-L4)
228	Assessment-Specific	Was the site assessed specific to the site loaded? Coded as **yes** or **no**
229	Reliability	reliability (also called reproducibility or precision): code numbers reported in percent
230	Tester Blinded?	was tester blinded to treatment? coded as yes or no
231	EXERCISE PROGRAM	leave as is
232	Type of Exercise	type of exercise: coded as strength, aerobic, both, or other
233	Length	length (weeks) of training
234	Frequency	frequency of training (days/week)
235	Frequency-SD	standard deviation for frequency of training (days/week)
236	Frequency-range	range of frequency of training (days/week)
237	Intensity-VO	intensity of training: coded as a % of maximum oxygen consumption
238	Intensity-VO-SD	standard deviation for intensity of training (% maximum oxygen consumption)
239	Intensity range	range for intensity of training (% maximum oxygen consumption)
240	Duration	duration of training (minutes/session)
241	Duration-SD	standard deviation for duration of training (minutes/session)
242	Duration range	range for duration of training (minutes/session)
243	Total minutes	total minutes of training, the product of length x frequency x duration (automatically calculated)
244	Sets	number of sets completed per exercise: code mean number or range
245	Reps	number of reps completed per exercise: code mean number or range
246	%1RM	percentage of 1RM
247	Rest Bewteen Sets	amount of rest, in seconds, between sets
248	# Exercises	number of exercises performed: code mean number or range
249	Mode(s)	mode of training: coded as walking (W), jogging (J), cycling (C), swimming (S), aerobic dance (AD), stairclimbing (SC), Other (O)
250	Compliance	% of exercise sessions that subjects attended
251	Compliance-SD	standard deviation for % of exercise sessions that subjects attended
252	Code Time	Time it took to code study
253	Date Coded	Date study was coded
	Notes:	Unless otherwise, all data are coded as means.
	Notes:	ND means not reported, not able to code based on reporting method, or not applicable.
	Notes:	All columns that are automatically calculated may be overwritten with original data.

APPENDIX C
Codebook for IPD Meta-Analyses

Exercise and Bone Desnity Variables Coded for IPD Meta-Analysis

Column #	Code	Description
1	study	Author(s) of study
2	study id	Unique study identification number
3	group	group data is from - coded as exercise or control
4	subject id	Unique subject identification number
5	group_des	Expanded description of group - code as reported
6	site_gen	General site that bone mineral density was assessed - coded as radius, femur spine, wrist, total body other
7	site_spe	Specific site that bone mineral density was assessed - coded as lumbar-1-4, lumbar-2-4, femoral neck, trochanter, intertrochanter, Ward's triangle, distal radius, proximal radius, total body, other
8	other_site	Expanded description of bone mineral density sites assessed - Code as reported
9	I_bmd	Initial bone mineral density (gm/cm/2)
10	f_bmd	Final bone mineral density (gm/cm/2)
11	d_bmd	Difference in bone mineral density (gm/cm/2)
12	pd_bmd	Percent change in bone mineral density
13	use	Rows of data to average? - coded as yes or no
14	age	Age of subjects (years)
15	ht	Height of subjects (cm)
16	I_wt	Initial weight of subjects (kg)
17	f_wt	Final weight of subjects (kg)
18	d_wt	Difference in weight of subjects (kg)
19	I_bm	Initial body mass index (kg/m/2)
20	f_bm	final body mass index (kg/m/2)
21	d_bm	difference in body mass index (kg/m/2)
22	I_fat_c	Initial percent fat (calipers)
23	f_fat_c	Final percent fat (calipers)
24	d_fat_c	Difference in percent fat (calipers)
25	I_fat_d	Initial percent fat (dual energy x-ray absorptiometry or underwater weighing)
26	f_fat_d	Final percent fat (dual energy x-ray absorptiometry or underwater weighing)
27	d_fat_d	Difference in percent fat (dual energy x-ray absorptiometry or underwater weighing)
28	I_lbm	Initial lean body mass (kg)
29	f_lbm	Final lean body mass (kg)
30	d_lbm	Difference in lean body mass (kg)
31	I_vo2	Initial maximum oxygen consumption (ml/kg/min)
32	f_vo2	Final maximum oxygen consumption (ml/kg/min)
33	d_vo2	Difference in maximum oxygen consumption (ml/kg/min)
34	p_vo2	Percent change in maximum oxygen consumption (ml/kg/min)
35	I_hr	Initial resting heart rate (beats/minute)

Exercise and Bone Desnity Variables Coded for IPD Meta-Analysis

Column #	Code	Description
36	f_hr	Final resting heart rate (beats/minute)
37	d_hr	Difference in resting heart rate (beats/minute)
38	p_hr	Percent change in resting heart rate
39	men_cyc	Length of menstrual cycle (days)
40	estrogen	Were subjects taking estrogen - coded as yes, no, or nd
41	estrogen2	Number of years subjects were taking estrogen
42	menarche	Age at menarche
43	meno	Menopausal status of subjects - coded as premenopausal, postmenopausal, or nd
44	meno_yrs	Number of years subjects were postmenopausal
45	gender	Gender of subject - coded as female or male
46	race	Race of subject - coded as white, black, hispanic, japanese, chinese, or other
47	smok_1	Did the subjects smoke? Coded as yes, no or nd
48	smok_2	Number of cigarettes smoked by subject each day
49	alcoh_1	Did the subjects consume alcohol? Coded as yes, no, or nd
50	alcoh_2	Number of alcoholic drinks consumed per day by subjects
51	fracture	Did the subjects have previous fractures prior to taking part in the study?
52	str_pc	Percent change in strength of the subjects
53	I_kcal	Initial number of calories consumed per day by subjects
54	f_kcal	Final number of calories consumed per day by subjects
55	d_kcal	Difference in number of calories consumed per day by subjects
56	pd_kcal	Percent difference in the number of calories consumed per day by subjects
57	I_fat	Initial fat intake of subjects (grams)
58	f_fat	Final fat intake of subjects (grams)
59	d_fat	Difference in fat intake of subjects (grams)
60	pd_fat	Percent difference in fat intake of subjects
61	I_cho	Initial cholesterol intake of subjects (milligrams)
62	f_cho	Final cholesterol intake of subjects (milligrams)
63	d_cho	Difference in cholesterol intake of subjects (milligrams)
64	pd_cho	Percent difference in cholesterol intake of subjects
65	I_prot	Initial protein intake of subjects (grams)
66	f_prot	Final protein intake of subjects (grams)
67	d_prot	Difference in protein intake of subjects (grams)
68	pd_prot	Percent difference in protein intake of subjects
69	I_ca	Initial calcium intake of subjects (milligrams)
70	f_ca	Final calcium intake of subjects (milligrams)
71	d_ca	Difference in calcium intake of subjects (milligrams)

Exercise and Bone Desnity Variables Coded for IPD Meta-Analysis

Column #	Code	Description
72	pd_ca	Percent difference in calcium intake of subjects
73	I_mg	Initial magnesium intake of subjects (milligrams)
74	f_mg	Final magnesium intake of subjects (milligrams)
75	d_mg	Difference in magnesium intake of subjects (milligrams)
76	pd_mg	Percent difference in magnesium intake of subjects
77	I_phos	Initial phosphorus intake of subjects (milligrams)
78	f_phos	Final phosphorus intake of subjects (milligrams)
79	d_phos	Difference in phosphorus intake of subjects (milligrams)
80	pd_phos	Percent difference in phosphorus intake of subjects (milligrams)
81	I_vitd	Initial vitamin D intake of subjects (I.U.'s)
82	f_vitd	Final vitamin D intake of subjects (I.U.'s)
83	d_vitd	Difference in vitamin D intake of subjects (I.U.'s)
84	pd_vitd	Percent difference in vitamin D intake of subjects
85	I_iron	Initial iron intake of subjects (milligrams)
86	f_iron	Final iron intake of subjects (milligrams)
87	d_iron	Difference in iron intake of subjects (milligrams)
88	pd_iron	Percent difference in iron intake of subjects
89	length	Length of the exercise protocol (weeks)
90	type	Type of training - Coded as weightbearing, non-weightbearing, weight training
91	comply	Percentage of exercise sessions that the subjects attended
92	assess	Type of bone mineral density assessment - Coded as dual energy x-ray absorptiometry (DEXA), dual photon absorptiometry (DPA), singel photon absorptiometry (SPA), quantitative computed tomography (QCT), or other
93	design	Study design coded as randomized controlled trial (RCT) or controlled trial (CT)
94	t_code	Time to code each study (hours and minutes)
95	d_code	Date study was coded

APPENDIX D
Publications in Peer-Reviewed Biomedical Journals

J Appl Physiol
88: 1730–1736, 2000.

Exercise and bone mineral density in men: a meta-analysis

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Kelley, George A., Kristi S. Kelley, and Zung Vu Tran. Exercise and bone mineral density in men: a meta-analysis. *J Appl Physiol* 88: 1730–1736, 2000.—The purpose of this study was to use the meta-analytic approach to examine the effects of exercise on bone mineral density (BMD) in men. A total of 26 effect sizes (ES) representing 225 subjects from 8 studies met the criteria for inclusion. When BMD sites assessed were specific to the sites loaded during exercise, increases of ~2.6% (2.1% in the exercisers and −0.5% in the controls) were found. These results were statistically significant (ES = 0.213, 95% bootstrap confidence interval = 0.007–0.452). Statistically significant ES changes were found for older (>31 yr) but not younger (<31 yr) adults, with differences between groups statistically significant (P = 0.04). Statistically significant changes were also observed at the femur, lumbar, and os calcis sites. The results of this study suggest that site-specific exercise may help improve and maintain BMD at the femur, lumbar, and os calcis sites in older men. However, the biological importance of the small changes observed for most outcomes, quality of studies, and limited data pool prevent us from forming any firm conclusion regarding the use of exercise for maintaining and/or improving BMD in men. Clearly, a need exists for additional studies.

men; osteoporosis; systematic review; review; physical activity

OSTEOPOROSIS AND LOW BONE mass are major public health problems affecting ~23,000,000 women ≥50 yr of age in the United States (28). However, osteoporosis and low bone mass are also a major public health problem among men, affecting ~5,000,000 individuals ≥50 yr of age in the United States (28). Approximately 5% of white, Asian, Hispanic, and American-Indian men 50–79 yr of age have osteoporosis, whereas 3.5% of black men 50–79 yr of age have the disease (28). For those individuals ≥80 yr of age, these numbers increase to ~24% among white men, 17% among black men, and 5% among Asian, Hispanic, and American-Indian men (28). In addition, it has been estimated that osteoporosis-related fractures represent 3% of all Medicare costs and that the lifetime risk of an osteoporotic fracture for white men ≥50 yr of age is ~13% (33).

However, this lifetime risk may be an underestimate, inasmuch as a recent study in Australia found that the residual lifetime fracture risk in 60-yr-old men with average life expectancy was 29% (18).

Exercise has been recommended as a nonpharmacological approach for maximizing bone mineral density (BMD) during the younger years as well as improving bone density by increasing and/or preventing the loss of bone during the older years (35). Exercise may be especially appropriate, since it is a low-cost intervention that is available to most of the general public. However, training studies examining the effects of exercise on BMD in men have led to conflicting results (2, 4–6, 13, 23–25, 31, 36). For example, of the 10 studies previously cited, only 39% of the sites assessed were reported as statistically significant and positive compared with a control group. One of the possible reasons for the lack of statistically significant results may be the small sample size that comprised many of these trials. As a result, the ability to detect meaningful differences may have been compromised. Meta-analysis is a quantitative approach in which individual study findings addressing a common problem are statistically integrated and analyzed (8, 14, 16, 29). It has been shown to be more accurate than the vote-counting approach (15) and may be especially useful when the number of studies is small and/or the sample sizes within each study are small (29). Although several meta-analyses have been conducted on the effects of exercise on bone density in women (3, 19–21, 37), we are not aware of any meta-analytic work dealing with the effects of exercise on BMD in men. Given the health-care consequences of low BMD in men and the potential for exercise to improve BMD, a need exists to use a quantitative approach to examine the effects of exercise on BMD in this population. Thus the purpose of this study was to use the meta-analytic approach to examine the effects of exercise on BMD in men.

METHODS

Data Sources

Computerized literature searches of articles indexed between January 1966 and December 1998 were performed using MEDLINE, Current Contents, Sport Discus, and Dissertation Abstracts International databases. The following keywords were used alone or in various combinations for computer searches: bone, exercise, physical activity, men, males, physical fitness, fitness, and osteoporosis. The titles and abstracts of studies identified in the computerized searches were examined to exclude any that were clearly irrelevant. The full text of the remaining articles was retrieved, and each paper was read to determine whether it contained information on the topic of interest. Because computer searches have

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been shown to yield fewer than two-thirds of relevant articles (9), the reference lists from original and review articles were also reviewed to identify any studies that had not been previously identified and appeared to contain information on the topic of interest. Hand searching of selected journals was also performed. Furthermore, three experts on exercise and BMD (Dr. Charlotte Sanborn, Dr. David Nichols, and Dr. Christine Snow) reviewed our reference list and coding sheet for thoroughness and completeness.

Study Selection

Inclusion criteria for this study were as follows: *1*) randomized or nonrandomized trials that included a comparative nonexercise control group, *2*) exercise as the only intervention, *3*) adult men (mean study age ≥18 yr) as subjects, *4*) journal articles, dissertations, and masters theses published in the English-language literature, *5*) studies published and indexed between January 1966 and December 1998, *6*) BMD (relative value of bone mineral per measured bone area) assessed, and *7*) training studies lasting ≥16 wk. Only information that met the above criteria was included in our analysis. Thus, for example, if BMD was also assessed in women, we did not include this information, since it did not meet our inclusion criteria. Because dissertations may eventually become full-length journal articles, we cross-referenced between the two to avoid duplication. We did not include abstracts and conference papers from national meetings because of the paucity of data provided as well as the inability to obtain complete data from the authors. Studies published in foreign language journals were also not included because of the potential error in the translation and interpretation of findings. Studies that met our inclusion criteria were also examined to ensure that the same subjects were not included in more than one study (11). For the two studies that met our inclusion criteria but did not provide appropriate information on changes in BMD (4, 23), personal contact was made with the authors to retrieve such information.

Data Extraction

Coding sheets that could hold 242 items were developed and utilized in this investigation. In addition, coding instructions that described how to code each item on the coding sheet were developed and utilized. To avoid inter- and intracoder bias, all data were independently extracted by two authors. The authors then met and reviewed every data point for accuracy and consistency. Disagreements were resolved by consensus. The major categories of variables coded included study characteristics, physical characteristics of subjects, and primary and secondary outcomes.

Statistical Analysis

Primary outcomes. The primary outcome in this study was changes in BMD. Because of the various ways in which the authors reported data on changes in BMD and because we also wanted to maximize the number of studies and outcomes that could be included in our analysis, we used the standardized difference approach as our effect size (ES) measure. This measure provides one with a statistic similar to a *z*-score. Each ES was calculated by subtracting the change outcome (percent or absolute) in the exercise group from the change outcome in the control group and then dividing this difference by the pooled standard deviation of the exercise and control groups (16). The ES was then corrected for small-sample bias (16). For those studies that did not report change outcome variances, these were estimated using previously developed methods (12). In general, an ES of 0.20 is considered a small effect, 0.50 a moderate effect, and 0.80 a large effect (7). An ES of 0.50, for example, means that the exercise group differed from the control group by 0.5 SD in favor of the exercise group. By use of a *z*-score table, this means that the exercise group would do better than ~69% of the control group. Although the first metric of choice should be the one that has the most meaning to the reader, in this case, the percent change difference, we were unable to use this metric because of insufficient reporting of data for calculating within-group percent change variances for each study. However, to enhance interpretation, we also calculated percent change differences for each study. Because of the small sample size in this study, especially for subgroup analyses, bootstrap resampling (5,000 iterations) was used to generate 95% bootstrap confidence intervals (BCI) around mean ES changes for BMD (10). The bootstrap technique is a computer-intensive, nonparametric method of estimating the reliability of the original sample estimate, in this case, ES changes in BMD. By randomly drawing from the available sample, with replacement, samples the same size as the original are generated. Each time an observation is selected for a new sample, each of the elements of the original sample has an equal chance of being selected. This is similar to replicating each member of a sample 5,000 times (iterations). The main advantage of this approach is that the estimate desired is not based on some theoretical distribution but, rather, on the sample itself. This approach frees one from the constraints of the central limit theorem. The number of iterations chosen was based on previous research demonstrating that improvement of estimation accuracy was limited beyond 5,000 iterations (38). If the 95% confidence interval included zero (0.00), it was concluded that there was no statistically significant effect of exercise on BMD.

Heterogeneity of ES changes in BMD was examined using the Q statistic (16). A random-effects model was used if changes were significantly heterogeneous ($P \leq 0.05$), whereas a fixed-effects model was used in the absence of significant heterogeneity (26).

For studies that included multiple outcomes because of more than one group, net changes were initially treated as independent data points. However, to examine the influence (sensitivity) of each study on the overall results, analyses were performed with each study deleted from the model.

Publication bias (the tendency for journals and/or authors to publish studies that yield statistically significant results) was examined using Kendall's τ statistic (1). A statistically significant result ($P \leq 0.05$) was considered to be suggestive of publication bias. In addition, we used a semiquantitative approach (funnel plot) to examine potential publication bias (22). This was accomplished by plotting the sample size on the vertical axis and changes in blood pressure on the horizontal axis. Usually, smaller studies will be more dispersed at the bottom of the funnel, whereas larger studies will be more congregated at the top. A gap at the bottom of the funnel on the left side indicates that small studies yielding null or negative results may be missing.

Study quality was assessed using a three-item questionnaire designed to assess bias, specifically, randomization, blinding, and withdrawals/dropouts (17). The number of points possible ranged from a low of 0 to a high of 5. All questions were designed to elicit yes (1 point) or no (0 points) responses. The questionnaire took <10 min/study. The questionnaire has been shown to be valid (face validity) and reliable (researcher-interrater agreement, $r = 0.77$, 95% confidence interval = 0.60–0.86) (17).

Subgroup analyses. Subgroup analyses for primary outcomes were performed using ANOVA-like procedures for

meta-analysis (16). These procedures provide statistics for within (Q_w)- and between (Q_b)-group differences. If statistically significant within-group (Q_w) heterogeneity existed ($P < 0.05$), a random-effects model was used. If no statistically significant within-group (Q_w) heterogeneity existed, a fixed-effects model was used. ES changes in BMD were initially examined when the data were partitioned according to whether the BMD sites assessed were specific to the sites loaded during the exercise protocol. Subgroup analysis was also performed when the data were partitioned according to the age of the subjects (≤31 vs. >31 yr of age), limited to those results in which the BMD sites assessed were specific to the sites loaded. We chose 31 yr of age as our cut point because it has been reported that peak bone mass is attained as late as ~30 yr of age (32). Further analyses were performed on site-specific results for older subjects in relation to specific assessment location (femur, lumbar, os calcis) and study design (randomized controlled trial vs. nonrandomized controlled trial). Bootstrap resampling (5,000 iterations) (10) was used to generate 95% confidence intervals around ES changes for all subgroups. Randomization tests (5,000 iterations) were used to generate probability values for between-group differences (30). Randomization tests using 5,000 iterations can detect a probability as low as 0.002 (30).

Regression analysis. Potential associations between ES changes in BMD and initial BMD and length of training were examined using regression procedures previously described by Hedges and Olkin (16).

Secondary outcomes. Secondary outcomes (changes in body weight, body mass index, percent body fat, lean body mass, maximum oxygen consumption, resting heart rate, calcium intake) were calculated as the difference (exercise minus control) of the changes (initial minus final) in these mean values. The original metric was used for all secondary outcomes. For those studies in which variance estimation was necessary, these were accomplished using the same procedures used to estimate variances for BMD (12). Fixed- and random-effects models were used following the same procedures described for BMD.

Unless otherwise noted, values are means ± SD. The α-level for statistical significance was set at $P \leq 0.05$. Bonferroni adjustments were not made because of the increased risk of a type II error.

RESULTS

Study Characteristics

A total of 3,141 titles and abstracts were reviewed. From those, 26 ES representing a total of 225 subjects (135 exercise, 90 control) and 18 groups (10 exercise, 8 control) from 8 studies met the criteria for inclusion (2, 5, 6, 13, 24, 25, 31, 36). The per person time to code each study once ranged from 0.67 to 2.63 h (1.04 ± 0.66 h). Two studies were not included because we were unable to obtain data necessary for the calculation of an ES (4, 23). Thus our percent loss that met our inclusion criteria was 20. One study (34) was not included because it contained some of the same subjects from another study that met our inclusion criteria (24). We chose to include the latter study because more complete data were available for extraction. A general description of the studies is shown in Table 1. Four studies were conducted in the United States (5, 24, 25, 36), two in Australia (2, 31), and one each in Japan (13) and the United Kingdom (6). For the five studies that reported such information (2, 6, 24, 31, 36), percent dropout, defined as the number of subjects who did not complete the study, ranged from 0 to 31% in the exercise groups (10 ± 12%) and from 0 to 22% in the control groups (5 ± 10%). The number of subjects in which pre- and post-BMD measures were assessed and included in our analysis ranged from 3 to 28 in the exercise groups (14 ± 8) and from 7 to 21 in the control groups (11 ± 6). Study quality ranged from 0 to 3 (1 ± 1). Compliance, defined as the percentage of exercise sessions attended, was >90% for the two studies that reported this information (13, 24). Reliability for BMD assessment (coefficient of variation) ranged from 0.4 to ~5.0% (1.5 ± 1.0%).

Physical Characteristics of Subjects

A description of the physical characteristics for the exercise and control groups may be found in Table 2. Only one study reported that calcium supplementation was given to subjects (13). For the four studies that reported such information, three reported that none of the subjects was taking any type of pharmacological intervention other than calcium that could affect BMD (2, 6, 13), and one (5) reported that subjects were taking drugs that could affect BMD. For the two studies that reported information on cigarette smoking, one reported that none of the subjects smoked cigarettes (24), and another reported that some of the subjects smoked (13). Three studies reported that subjects had not been physically active before participation in the study (5, 13, 24), whereas it appeared that another study included subjects that had been previously active (2). The two studies that reported information on previous fractures reported that subjects had not had previous fractures at the site(s) assessed before participation in the study (24, 25). None of the studies reported information on the alcohol intake of the subjects.

Primary Outcomes

Individual ES changes for primary outcomes (changes in BMD) are shown in Table 3. Approximately 39% of the 26 ES were reported as statistically significant and positive by the authors. Initial BMD values for all sites assessed ranged from 0.700 to 1.400 g/cm^2 in the exercise groups (1.120 ± 0.188 g/cm^2) and from 0.670 to 1.290 g/cm^2 in the control groups (1.078 ± 0.168 g/cm^2). With use of a random-effects model because of statistically significant heterogeneity ($Q = 45.01$, $P = 0.008$), overall ES changes were not statistically significant (ES = 0.028, 95% BCI = −0.166 to 0.230). ES changes were equivalent to an exercise-minus-control improvement of 2% (1.6% increase in the exercising subjects and 0.4% decrease in the controls). With each study deleted from the model once, ES changes ranged from a low of 0.028 (95% BCI = −0.166 to 0.230) to a high of 0.199 (95% BCI = −0.131 to 0.489). Although there was no quantitative evidence supporting publication bias ($r = -0.23$, $P = 0.10$), funnel plot analysis was suggestive of this potential form of bias.

Table 1. *General description of included studies*

Study	Design/Subjects	Intervention	BMD Assessment
Bennell et al. (2)	CT that included 2 different male exercise groups (27 power athletes, 31 endurance athletes) and 27 male controls 17–26 yr of age	12 mo of participation in power (sprinting, jumping, multievents) or endurance (middle- or long-distance) sports	DEXA (Hologic QDR 1000W) at upper limb, lumbar spine (L_1–L_4), femur, and tibia/fibula
Braith et al. (5)	RCT consisting of 16 male heart transplant patients assigned to exercise ($n = 8$, 56 ± 6 yr) or control ($n = 8$, 52 ± 10 yr) group	6 mo of lumbar extension exercises 1 day/wk and 2 days/wk of upper and lower body resistance training consisting of 1 set of 10–15 repetitions at 50% of 1 RM for each exercise (10 exercises total)	DEXA (Lunar) at femoral neck, lumbar spine (L_2–L_3), and total body
Cohen et al. (6)	CT consisting of 17 male novice college oarsmen (age 19.5 ± 2.4 yr) and 8 age- and gender-matched controls (19.3 ± 1.6 yr)	7-mo training program consisting of rowing (8 h/wk), weight training (1 h/wk), and running (1 h/wk)	DEXA (Lunar DPX) at lumbar spine (L_1–L_4), femoral neck, greater trochanter, and Ward's triangle
Fujimura et al. (13)	CT consisting of 15 previously sedentary male subjects (23–31 yr) assigned to an exercise ($n = 8$, 24.6 ± 2.83 yr) or control ($n = 7$, 26.4 ± 3.17 yr) group	4 mo of resistance training performed 3 times/wk and consisting of 2–3 sets of 10 repetitions at 60–80% of 1 RM for 7–8 exercises/session	DEXA (DCS-3000) at lumbar spine, femoral neck, midradius, and total body
Menkes et al. (24)	CT consisting of 18 previously sedentary male subjects (50–70 yr) assigned to exercise ($n = 11$, 59 ± 7.2 yr) or control ($n = 7$, 55 ± 2.65 yr) group	4 mo of resistance training performed 3 times/wk and consisting of 1 set of upper body and 2 sets of lower body exercises performed for 15 repetitions for each exercise	DEXA (Lunar DPX) at lumbar spine (L_2–L_4), femoral neck, and total body
Michel et al. (25)	CT that included 10 male runners (65.3 ± 7.91 yr) and 10 age- and gender-matched controls (64.5 ± 7.27 yr)	5 yr of running partitioned by groups that decreased their mileage by >20% vs. <20% over 5-yr period	QCT (GE9800) at lumbar spine
Pritchard et al. (31)	RCT that included 40 overweight male subjects assigned to exercise ($n = 21$, 44.9 ± 6.5 yr) or control ($n = 19$, 43.3 ± 4.5 yr) group	1 yr of aerobic exercise of choice (walking, jogging, swimming, stationary cycling) performed ≥3 times/wk for 30 min at 65–75% of maximum heart rate	DEXA (Hologic QDR 1000W) of total body
Williams et al. (36)	CT consisting of 20 exercising men (38–68 yr, mean 49.2) and 10 male controls (41–58 yr, mean 47.0)	9 mo of a marathon training program partitioned into groups that ran ~21.9 and 10 miles/wk, respectively	SPA at right central os calcis

Values are means ± SD. BMD, bone mineral density; DEXA, dual-energy X-ray absorptiometry; SPA, single-photon absorptiometry; QCT, quantitative computed tomography; CT, controlled trial; RCT, randomized controlled trial; RM, repetition maximum.

Subgroup Analyses

When data were partitioned according to whether the BMD sites assessed were specific to the sites loaded during the exercise protocol, statistically significant within-group changes were found when the sites assessed were specific to the site loaded (ES = 0.213, 95% BCI = 0.007–0.452) but not when the sites assessed were not specific to the sites loaded (ES = −0.205, 95% BCI = −0.613 to 0.219). ES changes in BMD were equivalent to exercise-minus-control increases of ~2.6% (2.1% in the exercisers and −0.5% in the controls) when the sites assessed were specific to the sites loaded and ~0.3% (−0.06% in the exercisers and −0.3% in the controls) when the sites assessed were not specific to the sites loaded. Although it was not statistically significant, there was a trend for between-group changes to be greater when the sites assessed were specific to the sites loaded ($Q_b = 3.02$, $P = 0.10$). Further subgroup analyses were then performed by limiting analyses to only those sites in which the assessment of BMD was specific to the sites loaded. These are shown in Table 4. Within-group analysis demonstrated that statistically significant increases were found for older but not younger adults and that the differences between groups were statistically significant. These changes were equivalent to an exercise-minus-control improvement of ~6.7% for older subjects (4.2% increase in exercise groups and 2.5% decrease in controls) and 0.4% increase in younger subjects (1% increase in exercisers and 0.6% increase in controls). When the one study that

Table 2. *Initial physical characteristics*

Variable	Exercise		Control	
	n	Mean ± SD	*n*	Mean ± SD
Age, yr	10	40.8 ± 17.9	8	41 ± 17.0
Height, cm	9	176.2 ± 4.2	7	174.6 ± 3.7
Weight, kg	9	76.0 ± 6.4	7	78.1 ± 9.2
BMI, kg/m^2	9	24.6 ± 2.6	7	25.7 ± 3.4
Fat, %	5	17.0 ± 7.6	4	21.1 ± 6.7
LBM, kg	5	60.6 ± 4.7	4	58.9 ± 5.25
Calcium, mg/day	4	1,090 ± 259	3	892 ± 95

n, Number of groups reporting data; BMI, body mass index; LBM, lean body mass.

Table 3. *Individual ES from studies*

Study	Sites Assessed	No. Assessed	ES(d)	Var(d)
Bennell et al. (2)	Upper limb (power athletes)	42	−0.185	0.096
	Lumbar spine L_1–L_4 (power athletes)	42	0.844	0.107
	Femur (power athletes)	42	0.042	0.095
	Tibia/fibula (power athletes)	42	−0.222	0.096
	Upper limb (endurance athletes)	49	−0.199	0.084
	Lumbar spine L_1–L_4 (endurance athletes)	49	0.344	0.085
	Femur (endurance athletes)	49	−0.343	0.085
	Tibia/fibula (endurance athletes)	49	0.034	0.083
Braith et al. (5)	Total body	16	0.877	0.282
	Femoral neck	16	0.705	0.271
	Lumbar spine L_2–L_3	16	1.569	0.353
Cohen et al. (6)	Lumbar spine L_1–L_4	25	0.879	0.207
	Femoral neck	25	−0.257	0.186
	Greater trochanter	25	−0.568	0.194
	Ward's triangle	25	−0.265	0.186
Fujimura et al. (13)	Total body	15	−0.025	0.268
	Lumbar spine	15	−0.141	0.269
	Femoral neck	15	−0.203	0.270
	Midradius	15	0.807	0.297
Menkes et al. (24)	Total body	16	−0.126	0.255
	Lumbar spine L_2–L_4	16	0.099	0.254
	Femoral neck	16	0.270	0.257
Michel et al. (25)	Lumbar spine L_1 (<20% decrease)	13	0.858	0.465
Pritchard et al. (31)	Total body	40	−1.010	0.118
Williams et al. (36)	Os calcis (22 miles/wk)	17	1.048	0.284
	Os calcis (10 miles/wk)	23	0.260	0.179

No. assessed, sum of exercise and control subjects in which BMD was assessed; ES(d), effect size (ES) corrected for small sample bias; Var(d), variance of ES(d); <20%, <20% decrease in running mileage over course of study.

yielded two ES from heart transplant patients in the older group was deleted from the model, statistically significant within-group effects were again observed for older (ES = 0.442, 95% BCI = 0.207–0.799) but not younger (ES = 0.066, 95% BCI = −0.158 to 0.333) subjects. However, no statistically significant differences were observed between groups (Q_b = 2.26, P = 0.23). ES changes were equivalent to exercise-minus-control improvements of ~4.0% in older subjects (2% increase in exercisers and 2% decrease in controls). With ES results limited to only older adults, statistically significant within-group ES were found at the femur, lumbar, and os calcis sites, with no statistically significant between-group differences observed. ES changes in BMD were equivalent to exercise-minus-control improvements of ~5.9% at the femur site (4% increase in exercisers and 1.9% decrease in controls), 10.7% at the lumbar site (5.8% increase in exercisers and 4.9% decrease in controls), and 1.6% at the os calcis site (2.1% increase in exercisers and 0.5% increase in controls). With the one study in heart transplant patients deleted, there was an exercise-minus-control improvement of ~6.1% in lumbar BMD (1.0% in exercisers and −5.1% controls). Statistically significant within-group ES increases in BMD were also found when data were partitioned by study design. This was equivalent to exercise-minus-control improvements of ~13.5% for randomized trials (9.8% increase in exercisers and 3.7% decrease in controls) and 4.2% for nonrandomized trials (2% increase in exercisers and 2.2% decrease in controls). However, the percent changes found for randomized controlled trials were derived from the one study in heart transplant patients. No statistically significant ES differences were observed between groups.

Regression Analysis

No statistically significant associations were found between ES changes in BMD and length of training or initial BMD.

Secondary Outcomes

No statistically significant differences were found for any of the secondary outcomes. These included body weight (−0.3 kg, 95% BCI = −2.2 to 0.79 kg), body mass index (−0.9 kg/m^2, 95% BCI = −0.9 to 0.1 kg/m^2), and lean body mass (0.3 kg, 95% BCI = −0.2 to 0.6). Insufficient data were provided to assess changes in percent fat, maximum oxygen consumption, resting heart rate, and calcium intake.

Table 4. *Subgroup analyses*

Variable	No. of Studies	No. Assessed	No. of ES	ES(d)	95% BCI	Q_b
Age + site specific						
Older (<31 yr)	4	85	7	0.605	0.324 to 1.032	5.89 (0.04)*
Younger (≤31 yr)	4	131	13	0.066	−0.157 to 0.312	
Location + site specific (older only)						
Femur	2	32	2	0.482	0.270 to 0.705	0.32 (0.86)
Lumbar	3	45	3	0.749	0.099 to 1.327	
Os calcis	1	40	2	0.565	0.260 to 1.048	
Design + site specific (older only)						
RCT	2	56	2	1.082	0.705 to 1.569	1.98 (0.24)
CT	3	69	5	0.442	0.204 to 0.799	

No. assessed, sum of exercise and control subjects in which BMD was assessed; BCI, bootstrap confidence interval; Q_b, differences between groups, with P values in parentheses. *Statistically significant, $P < 0.05$.

DISCUSSION

The results of this study suggest that site-specific exercise may help improve and maintain BMD in older men. These results also support the notion that changes in BMD are specific to the sites loaded during exercise in older men. However, these results should be interpreted with caution, inasmuch as they were based on a very limited data pool. Perhaps little change was seen in BMD among younger subjects because subjects already possessed optimal levels of BMD and/or the loss of BMD generally occurs during the later, rather than during the younger, years. In addition, it may also be that more subjects in the older group had been sedentary for a longer period or were not able to ambulate very much. This may be especially true for the one study that included heart transplant patients, because when we deleted this study from our subgroup analysis the increase in BMD in the exercise group decreased from ~6% to 1% (5).

The fact that exercise is an inexpensive, nonpharmacological approach that is available to most of the general public makes this form of treatment appealing, especially given the other physiological and psychological benefits that may be derived from participation in exercise. However, it is important to realize that ~60% of adults in the United States do not regularly participate in adequate amounts of physical activity (27). Furthermore, only 16% of the US population between the ages of 18 and 64 yr report that they regularly participate in progressive-resistance exercise (27). In addition, one must also consider the potential adverse effects of exercise, e.g., arthritis, injury, and cardiac events. Unfortunately, we were unable to determine any potential adverse effects of exercise in this meta-analysis because only one study, limited to heart transplant patients, reported such information (5). The authors concluded that the exercise intervention was safe because it was not associated with an increase in rejection (5). Thus, although participation in a regular exercise program may be efficacious for improving and/or maintaining BMD in men, it may not be very effective in the "real world." Consequently, alternative nonpharmacological and pharmacological interventions for increasing and/or maintaining BMD may be necessary.

Despite the positive results observed in this study, the biological importance of these small changes might not be sufficient to recommend exercise alone as a nonpharmacological intervention. Because the primary reason for improving and/or maintaining BMD is to reduce fracture risk, one would like to know how much of an increase or prevention of loss in BMD is necessary to reduce the incidence of fracture. A recent longitudinal study has shown that femoral neck BMD in men was 24% lower in those with hip fractures and 12% lower in those with fractures of the vertebrae and upper limb (28a). The study also found that a decrease of 1 SD in femoral neck BMD was associated with a 2.3, 1.9, and 1.5 increase in the odds of fracture at the hip, vertebrae, and upper limbs, respectively (28a). The smaller results observed in our study suggest that if exercise is recommended, it should be done only in conjunction with other types of nonpharamcological and/or pharmacological interventions. Furthermore, we are not aware of any consensus as to how exercise-induced increases in BMD affect bone strength. For example, the implications of bone mass laid down on periosteum vs. endosteum may differ in relation to altering bone strength.

A second factor that warrants caution in the interpretation of our results is the relatively low quality of the studies included in our analysis. For example, only one study received a score of 3 while the remaining studies received scores ranging from 0 to 2. In addition, the different types of exercise interventions varied considerably. Furthermore, the fact that our funnel plot analysis was indicative of publication bias suggests that the results of this study may be an overestimate of the effects of exercise on BMD in men. Ideally, to examine the efficacy and effectiveness of exercise on BMD in men, it is suggested that future studies *1*) randomize subjects to an exercise and control condition, *2*) blind the person responsible for the assessment of BMD to the treatment assignment of subjects, *3*) limit participation to only subjects who have been previously sedentary, *4*) include weight-bearing exercise protocols that are reflective of those in which the population will be able to participate, *5*) assess BMD at the sites that were loaded during the exercise protocol, and *6*) include efficacy as well as effectiveness (intention-to-treat) analysis. In addition, it would be beneficial to examine any changes in BMD that might occur on cessation of exercise. Furthermore, it is critical that authors submit and be allowed to publish well-designed studies that yield null results. Consequently, we will be able to form a more valid conclusion regarding the true effects of exercise on BMD in men. Given the prevalence of low BMD in men $\geq$50 yr of age, it may be especially important to focus on this population (28).

Another factor that warrants caution in the interpretation of our results was the availability of data. Although meta-analysis is more quantitative than traditional narrative reviews, potential problems exist. The meta-analytic review, like any review, is limited by the available data. One potential problem in this investigation was the small number of ES available for some of the subgroup analyses. For example, ES changes in BMD at the specific sites we were able to examine (femur, lumbar, os calcis) were limited to two or three outcomes per site.

Despite our resampling approach because of the small sample sizes available for many of the analyses, additional studies in this area are needed before any firm conclusions can be made regarding the efficacy and effectiveness of exercise as a nonpharmacological intervention for improving and/or maintaining BMD in men. In addition, insufficient information was available to examine results according to the impact of the exercise protocols on the BMD sites assessed. Future studies need to provide a complete description of the exercise intervention.

In conclusion, the results of this study suggest that site-specific exercise may help increase and/or maintain BMD at the femur, lumbar, and os calcis sites in older men. However, the biological importance of the relatively small changes observed for most outcomes, quality of studies included, and limited data pool prevent us from forming any firm conclusion regarding the use of exercise for maintaining and/or improving BMD in men.

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Research Series Article

Resistance Training and Bone Mineral Density in Women

A Meta-Analysis of Controlled Trials

ABSTRACT

Kelley GA, Kelley KS, Tran ZV: Resistance training and bone mineral density in women: a meta-analysis of controlled trials. *Am J Phys Med Rehabil* 2001;80:65–77.

The purpose of this study was to use meta-analysis to examine the effects of resistance training on bone mineral density at the femur, lumbar spine, and radius in pre- and postmenopausal women. Resistance training had a positive effect on bone mineral density at the lumbar spine of all women and at the femur and radius sites for postmenopausal women. It was concluded that resistance training has a positive effect on bone mineral density in women.

Key Words: Exercise, Bone, Women, Meta-Analysis

Osteopenia and osteoporosis are major public health problems in the United States, affecting primarily lean, white, postmenopausal women.[1] Currently approximately 26.2 million white, postmenopausal women in the United States have either osteopenia or osteoporosis.[1] More specifically, osteopenia, defined as bone density that is 1 to 2.5 SD below the young adult reference range, affects an estimated 16.8 million (54%) of postmenopausal white women in the United States, whereas osteoporosis, defined as bone density >2.5 SD below the young adult reference range, affects another 9.4 million (30%) women.[1, 2] Low-bone density increases the risk for fractures, particularly at the hip, spine, and distal forearm. Currently, the estimated lifetime risk for fracture in 50-yr-old white women in the United States is 17.5% at the hip, 15.6% at the vertebrae, and 16.0% at the distal forearm.[1] In terms of the mortality rate, the survival rate at 5-yr follow-up relative to those of like age and gender is 0.83 for those who have experienced a hip fracture, 0.82 for vertebral fractures, and 1.00 for fractures of the forearm.[3] In the United States,

the estimated cost of fractures can be as high as $20 billion per year, with hip fractures accounting for more than a third of the total cost.[4] Furthermore, because of increased life expectancy, the number of women with low-bone density and subsequent fractures is expected to increase substantially in future years.

Physical activity has been suggested as a nonpharmacologic intervention for maximizing bone density during the younger years and preventing the bone loss during the later years.[5] Recent meta-analyses[6, 7] demonstrated the positive effects of aerobic exercise on both lumbar spine and hip bone mineral density (BMD) in postmenopausal women. Another potentially valuable type of physical activity is resistance training. Resistance training is a low-cost, nonpharmacologic intervention that is available to most of the public. Besides the positive effects on the bone, resistance exercise increases lean-body mass, decreases body fat, and increases muscular strength in both adult men and women.

Unfortunately, traditional narrative reviews on the effects of progressive resistance exercise on BMD have led to conflicting results. For example, seven reviews[8–14] have suggested that progressive resistance exercise *may* have a positive effect on BMD, although nine reviews[15–23] have suggested that progressive resistance exercise *does* have a positive effect. These discrepancies are not surprising given the fact that intervention studies[24–52] examining the effects of resistance exercise on BMD in adults have led to less than overwhelmingly positive results. For example, for the BMD sites assessed in previously mentioned studies, only 20% were reported as statistically significant. One of the possible reasons for the lack of statistically significant findings may be the result of the low statistical power leading to an increased risk of type 2 errors in some studies. Meta-analysis is a quantitative approach in which individual studies addressing a common problem are statistically aggregated.[53, 54] It is especially useful with a small number of subjects in the studies.[54]

As part of a larger study, we[55] previously showed a weight-training-induced improvement of approximately 1% in BMD at all sites combined in postmenopausal women. However, a detailed examination of the effects of progressive resistance exercise on BMD was not conducted. This is also the case with another meta-analysis[56] that combined BMD results from both progressive resistance and aerobic exercise studies. To date, we are unaware of any meta-analysis that has provided a detailed examination of the effects of resistance training on BMD in women. Given the healthcare consequences of low BMD, especially among women, it is important to gain a better understanding of the effects of resistance training on BMD. Thus, the purpose of this study was to use the meta-analytic approach to examine the effects of resistance training on BMD in women.

METHODS

Data Sources

We performed computerized literature searches of articles indexed between January 1966 and December 1998 using MEDLINE, Current Contents, Sport Discus, and Dissertation Abstracts International databases. The following keywords were used either alone or in combinations for computer searches: bone, bone density, bone mineral density, exercise, physical activity, women, females, physical fitness, fitness, weight training, resistance exercise, resistance training, osteoporosis, and osteopenia. The titles and abstracts of studies identified in the computerized searches were examined to exclude irrelevant studies. We retrieved the full text of the remaining articles and we read each paper to determine whether it contained information on the topic of interest. Because computer searches have been shown to yield less than two-thirds of relevant articles,[57] the reference lists from both original and review articles were also reviewed to locate studies that had not been previously identified and which seemed to contain information on the topic of interest. In addition, we also hand searched selected journals. Furthermore, three experts on exercise and BMD (Drs. Charlotte Sanborn, David Nichols, and Christine Snow) reviewed our reference list and coding sheet for thoroughness and completeness.

Study Selection

Inclusion criteria for this study were as follows: (1) randomized or nonrandomized trials that included a comparative nonexercise control group or control period; (2) resistance training, defined as any external resistance added while performing exercises, as the only intervention; (3) adult female humans (mean study age, $\geq$18 yr) as subjects; (4) journal articles, dissertations, and master's theses published in the English-language literature; (5) studies published and indexed between January 1966 and December 1998; (6) BMD (relative value of bone mineral per measured bone area) assessed at the femur, lumbar spine, or radius; (7) training studies lasting a minimum of 16 wk. Only information that met the above criteria was included in our analysis. Thus, for example, if BMD was also assessed in women performing aerobic exercise, we did not include this information because it did not meet our inclusion criteria. We limited our analysis to the femur, lumbar spine, and radius because they are the most often studied and these areas are the most vulnerable to fracture. Because dissertations may eventually become full-length journal articles, we cross-refer-

enced between the two to avoid duplication. We did not include abstracts and conference papers from national meetings because of the paucity of data provided as well as the inability to obtain complete data from the authors. Studies published in foreign language journals were also not included because of the potential error in the translation and interpretation of findings. Studies that met our inclusion criteria were also examined to ensure that the same subjects were not included in more than one study.[58] For studies that met our inclusion criteria but did not provide appropriate information on changes in BMD,[59, 60] we personally tried to contact the authors to retrieve such information.

Data Extraction

Coding sheets that could hold 242 items were developed and used in this investigation. In addition, coding instructions that described how to code each item on the coding sheet were developed and used. To avoid coding bias, all data were extracted independently by two authors. The authors then met and reviewed every item for accuracy and consistency. Disagreements were resolved by consensus. Blinding of coders to study information in relation to the identity and institutional affiliation of the study authors, as well as study results, were not performed because, according to a recent work,[61] these procedures have neither a clinically nor statistically significant effect on the results. The major categories of variables coded included study characteristics, physical characteristics of subjects, and primary and secondary outcomes.

Statistical Analysis

Primary Outcomes. The primary outcomes in this study were changes in BMD at the femur, lumbar spine, and radius. Because of the various ways in which the authors reported data on changes in BMD and because we also wanted to maximize the number of studies and outcomes that could be included in our analysis, we used the standardized difference approach as our effect size (ES) measure.[62] This was calculated by subtracting the change outcome in the exercise group from the change outcome in the control group, and then dividing this difference by the pooled standard deviation of the exercise and control groups.[62] The ES was then corrected for small-sample bias.[62] For studies that included multiple outcomes because of more than one group (for example, an exercise group that trained at a higher intensity *vs.* one that trained at a lower intensity), net changes in bone mineral density were treated as independent data points.[63] In general, an ES of 0.20 was considered a small effect, 0.50 a moderate effect, and 0.80 a large effect.[64] An ES of 0.20, for example, means that the exercise group differed from the control group by two-tenths of a standard deviation in favor of the exercise group. Because of the small-sample size in this study, especially for subgroup analyses, bootstrap resampling (5,000 iterations) was used to generate 95% BCIs around mean ES changes for BMD.[65] The bootstrap technique is a computer-intensive, nonparametric method of estimating the reliability of the original sample estimate, in this case, ES changes in BMD. By randomly drawing from the available sample, with replacement, samples the same size as the original are generated. Each time an observation is selected for a new sample, each of the elements of the original sample has an equal chance of being selected. This is similar to replicating each member of a sample 5,000 times (iterations). The main advantage of this approach is that the estimate desired is not based on some theoretical distribution, but rather, on the sample itself. This approach frees one from the constraints of the central limit theorem. The number of iterations chosen was based on previous research demonstrating that improvement of estimation accuracy was limited beyond 5,000 iterations.[66] If the 95% confidence interval included zero (0.00), it was concluded that there was no statistically significant effect of exercise on BMD.

Heterogeneity of ES changes in BMD was examined using the Q statistic.[62] A random-effects model was used when changes were significantly heterogeneous ($P < 0.05$), whereas a fixed-effects model was used in the absence of significant heterogeneity.[53] For studies that included multiple outcomes because of more than one group, net changes were treated initially as independent data points. However, to examine the influence (sensitivity) of each study on the overall results, analyses were performed with each study deleted from the model.

Publication bias (the tendency for journals to publish studies that yield statistically significant results and/or authors to only submit studies that yield statistically significant results) was examined using Kendall's tau statistic (τ).[67] A statistically significant result ($P < 0.05$) was considered to be suggestive of publication bias.

Study quality was assessed using a three-item questionnaire designed to assess bias, specifically, randomization, blinding, and withdrawals/dropouts.[68] The number of points possible ranged from a low of 0 to a high of 5. All questions were designed to elicit yes (1 point) or no (0 point) responses. The questionnaire took less than 10 min per study. The questionnaire has been shown to be both valid (face validity) and reliable (researcher interrater agreement, $r = 0.77$, 95% confidence interval = 0.60–0.86).[68]

Subgroup Analyses. For categorical variables, subgroup analyses for primary outcomes were performed using analysis of variance-like procedures for meta-analysis.[62] These procedures provide statistics for both

TABLE 1
Study characteristics

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Bouxsein[24]	RCT that included 20 premenopausal women ~20 yr old assigned to either a resistance training (n = 12) or control (n = 8) group	35 wk of training consisting of 14 exercises performed 3 times per week for 3 sets of 8–12 repetitions at 65–85% of 1 RM	DEXA (Hologic) at the lumbar spine (L2-4), femoral neck, trochanter, and Ward's triangle
Chilibeck et al.[25]	CT consisting of 30 premenopausal women assigned to either a resistance training (n = 20; age = 20.3 ± 1.0 yr) or control (n = 10; age = 20.2 ± 0.4 yr) group	20 wk of training consisting of 7 exercises performed 3 times per week for 5 sets of 6–12 repetitions at 70–80% of 1 RM	DEXA (Hologic) at the arms, ribs, thoracic spine, lumbar spine, pelvis, legs, whole body, femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip
Delaney[26]	RCT that included 88 premenopausal women ~28 to 39 yr of age assigned to either a resistance training (n = 46) or control (n = 42) group	20 wk of training consisting of 12 exercises performed 3 times per week for 3 sets of 8–12 repetitions at 70% of 1 RM	DEXA (Lunar) of the lumbar spine (L2-4) and total body; SPA (Lunar) at the radius
Dornemann et al.[27]	RCT consisting of 26 premenopausal women assigned to either a resistance training (n = 12; age = 43 ± 3 yr) or control (n = 14; age = 45 ± 3 yr) group	24 wk of training consisting of 7 exercises performed 3 times per week for 1–5 sets of 4–15 repetitions	DEXA (Hologic) at the lumbar spine, femoral neck, and distal radius
Gleeson et al.[28]	CT that included 72 premenopausal women assigned to either a resistance training (n = 34; age = 33.4 ± 6.3 yr) or control (n = 38; age = 32.7 ± 5.6 yr) group	52 wk of training consisting of 8 exercises performed 3 times per week for 2 sets of 20 repetitions at 60% of 1 RM	DPA (Lunar) at the lumbar spine; SPA (Osteon) at the os calcis
Hartard et al.[29]	CT that included 31 postmenopausal women with osteopenia assigned to either a resistance training (n = 16; age = 63.6 ± 6.2 yr) or control (n = 15; age = 67.4 ± 9.7 yr) group	24 wk of training performed 2 times per week for 1–2 sets of 8–12 repetitions at 70% of 1 RM	DEXA (Norland) at the lumbar spine (L2-4) and femoral neck
Heinonen et al.[30]	CT that included 32 premenopausal women assigned to either a resistance training (n = 13; age = 23.8 ± 5.0 yr) or control (n = 19; age = 25.7 ± 5.2 yr) group	52 wk of training consisting of 2 exercises performed 5 times per week for 5 sets of 10 repetitions at 80% of 1 RM	DEXA (Norland) at the proximal humerus, humeral shaft, radial shaft, ulnar, distal forearm, and calcaneus
Heinonen et al.[31]	RCT that included 53 perimenopausal women 52–53 yrs of age assigned to either a resistance training (n = 26) or control (n = 27) group	78 wk of calisthenics consisting of 8 exercises performed 4 times per week for 3 sets of 16 repetitions with the addition of ankle and wrist bands (1–2 kg)	DEXA (Norland) at the lumbar spine (L2-4), femoral neck, calcaneus, and distal radius
Kerr et al.[32]	RCT that included 42 postmenopausal women 40–70 yr of age assigned to either a muscular strength (n = 23) or muscular endurance (n = 19) group (nonexercising limb served as control)	52 wk of training consisting of 11 exercises performed 3 times per week for 3 sets of 8 repetitions (strength group) or 3 sets of 20 repetitions (endurance group)	DEXA (Hologic) at the femur (trochanter, intertrochanter, femoral neck, Ward's triangle) and radius (ultra distal, mid, and 1/3)
Little[33]	CT that included 10 postmenopausal women assigned to either a resistance training (n = 6; age = 59.5 ± 2.3 yr) or control (n = 4; age = 60.8 ± 1.4 yr) group	32 wk of training consisting of 9 exercises performed 3 times per week for 1 set of 8–12 repetitions at 60–80% of 1 RM	DPA (Lunar) at the lumbar spine (L2-4) and femoral neck; SPA (Lunar) at the distal radius
Lohman et al.[34]	RCT that included 56 premenopausal women assigned to either a resistance training (n = 22; age = 34.2 ± 2.6 yr) or control (n = 34; age = 34.4 ± 3.8 yr) group	78 wk of training consisting of 12 exercises 3 times per week for 3 sets of 8–12 repetitions at 70–80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, trochanter, Ward's triangle, and radius
Mayoux-Benhamou et al.[35]	RCT that included 33 postmenopausal women assigned to either a psoas training (n = 21; age = 58.2 ± 3.4 yr) or control (n = 12; age = 58.9 ± 1.3 yr) group	156 wk of daily psoas training consisting of 2–3 sets of 60 daily hip flexions with 5 kg on the knee	QCT (Elscint) at the lumbar spine (L1-4)

TABLE 1
Continued

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Nelson et al.[36]	RCT that included 39 postmenopausal women assigned to either a resistance training (n = 20; age = 61.1 ± 3.7 yr) or control (n = 19; age = 57.3 ± 6.3 yr) group	52 wk of training consisting of 5 exercises performed 2 times per week for 3 sets of 8 repetitions at 80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4) and femoral neck
Nichols et al.[37]	RCT that included 17 postmenopausal women at least 60 yr of age assigned to either an exercise (n = 9) or control (n = 7) group	52 wk of training consisting of 8 exercises performed 3 times per week for 3 sets of 10–12 repetitions at 80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, and trochanter
Notelovitz et al.[38]	RCT that included 20 surgically menopausal women assigned to either an estrogen + resistance training (n = 9; age = 43.3 ± 9.6 exercise yr) or estrogen + no exercise (n = 11; age = 46.2 ± 6.8 yr) group	52 wk of training consisting of up to 11 exercises performed 3 times per week for 8 repetitions per exercise	DPA (Lunar) at the spine as well as total body; SPA (Lunar) at the radius
Payne[39]	CT that included 48 premenopausal women assigned to either a resistance training (n = 28; age = 24.6 ± 9.2 yr) or control (n = 20; age = 22.8 ± 6.1 yr) group	18 wk of training consisting of 9 exercises performed 3 times per week for 1–6 sets of 6–10 repetitions per exercise	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, Ward's triangle, trochanter, and total body
Preisinger et al.[40]	RCT that included 58 postmenopausal women assigned to either an exercise (n = 27; age = 62.6 ± 5.9 yr) or control (n = 31; age = 59 ± 8 yr) group	208 wk of training consisting of 3 exercises performed 3 times per week for 3 repetitions	SPA (Osteodensitometer) at the mid and distal forearm
Protiva[41]	CT that included postmenopausal women 74–94 yr of age observed during a 6-mo control period (n = 13) and then assigned to 9 mo of resistance training (10 of the 13 completed the training along with an additional five subjects)	36 wk of training that included 8 exercises performed 3 times per week for 1–2 sets of 6–12 repetitions while wearing a weighted vest	DEXA (Hologic) at the femoral neck, trochanter, hip, and whole body
Pruitt et al.[42]	CT that included 26 postmenopausal women assigned to either a resistance exercise (n = 17; age = 53.6 ± 4.1 yr) or control (n = 9; age = 55.6 ± 2.9 yr) group	36 wk of training that included 11 exercises performed 3 times per week for one set of 10–15 repetitions at 50–60% of 1 RM	DPA (Lunar) at the lumbar spine (L2-4) and femoral neck
Pruitt et al.[43]	RCT that included 26 postmenopausal women assigned to either high-intensity resistance training (n = 8; age = 67 ± 0.5 yr), low-intensity resistance training (n = 7; age = 67.6 ± 1.4 yr) or control (n = 11; age = 69.6 ± 4.2 yr) group	52 wk of training that included 10 exercises performed 3 times per week for either 2 sets of 7 repetitions at 80% of 1 RM (high-intensity) or 3 sets of 14 repetitions at 40% of 1 RM (low-intensity)	DEXA (Hologic) at the lumbar spine (L2-4) and total hip (femoral neck, trochanter, and Ward's triangle)
Rockwell et al.[44]	CT that included 17 premenopausal women assigned to either a resistance training (n = 10; age = 36.2 ± 3.9 yr) or control (n = 7; age = 40.4 ± 11.5 yr) group	36 wk of training that included 8 exercises performed 2 times per week for 2 sets of 12 repetitions at 70% of 1 RM	DEXA (Lunar) at the lumbar spine and femoral neck
Shaw and Snow[45]	CT that included 40 postmenopausal women assigned to either a resistance training (n = 18; age = 64.2 ± 5.8 yr) or control (n = 22; age = 62.5 ± 6.6 yr) group	36 wk of training that included 6 exercises performed 3 times per week for 3–5 sets of 10–15 repetitions while wearing a weighted vest. Subjects also performed jumping exercises with a weighted vest.	DEXA (Hologic) at the lumbar spine (L2-4) and femoral neck
Sinaki et al.[46]	RCT that included 67 premenopausal women 30–40 yr of age assigned to either a resistance training (n = 32) or control (n = 35) group	156 wk of training that included exercises performed 3 times per week for 3 sets of 10 repetitions	DEXA (Hologic) at the lumbar spine (L2-4), trochanter, femoral neck, and Ward's triangle

TABLE 1
Continued

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Sinaki et al.[47]	RCT that included 65 postmenopausal women assigned to either a resistance training (n = 34; age = 55.6 ± 4.5 yr) or control (n = 31; age = 56.5 ± 4.5 yr) group	104 wk of back extension exercise performed 5 times per week for 1 set of 10 repetitions at 30% of maximal isometric back muscle strength	DPA at the lumbar spine (L2-4)
Smidt et al.[48]	RCT that included 49 postmenopausal women assigned to either a resistance training (n = 22; age = 56.6 ± 6.6 yr) or control (n = 27; age = 55.4 ± 8.0 yr) group	52 wk of training that included 3 exercises performed 3–4 times per week for 3 sets of 10 repetitions at 70% of 1 RM	DPA at the lumbar spine (L2-4), femoral neck, Ward's triangle, and trochanter
Snow-Harter et al.[49]	RCT that included 20 premenopausal women approximately 20 yr old assigned to either a resistance training (n = 12) or control (n = 8) group	32 wk of training that included 14 exercises performed 3 days per week for 3 sets of 8–12 repetitions at 65–85% of 1 RM	DEXA (Hologic) at the lumbar spine (L2-4), femoral neck, trochanter, and Ward's triangle
Taafe et al.[50]	RCT that included 25 postmenopausal women assigned to either a high-intensity resistance training (n = 7; age = 67.0 ± 0.5 yr), low-intensity resistance training (n = 7; age = 67.6 ± 1.3 yr), or control (n = 11; age = 69.6 ± 4.3 yr) group	52 wk of training that included 3 exercises performed 3 days per week for either 3 sets of 14 repetitions at 40% of 1 RM (low-intensity) or 2 sets of 7 repetitions at 80% of 1 RM (high-intensity)	DEXA (Hologic) at the femur and middle third of the femur
Thorvaldson[51]	RCT that included 50 postmenopausal women assigned to either a resistance training (n = 12; age = 54.6 ± 2.1 yr) or control (n = 21; age = 54.6 ± 2.1 yr) group	24 wk of training that included 6 exercises performed 3–5 days per week for 3 sets of 10 repetitions	DEXA (Hologic) at the lumbar spine (L1-4) and femoral neck; QCT at the distal radius
Vuori et al.[52]	CT that included 24 premenopausal women assigned to either a resistance exercise (n = 12; age = 21.0 ± 2.5 yr) or control (n = 12; age = 22.0 ± 3.0 yr) group	52 wk of training that included leg press exercise performed 5 times per week for 5 sets of 10 repetitions at 80% of 1 RM	DEXA (Norland) at the lumbar spine, femoral neck, distal femur, patella, proximal tibia, and calcaneus

RCT, randomized controlled trial; CT, controlled trial; subjects; ages reported as mean ± SD; number of subjects listed includes only those who completed the study; BMD, bone mineral density; 1 RM, one repetition maximum; DEXA, dual-energy x-ray absorptiometry; DPA, dual photon absorptiometry; SPA, single photon absorptiometry; QCT, quantitative computed tomography.

within (Q_w) and between (Q_b) group differences. If statistically significant within-group (Q_w) heterogeneity existed ($P < 0.05$), a random-effects model was used. If no statistically significant within-group (Q_w) heterogeneity existed, a fixed-effects model was used. ES changes in BMD were examined initially when the data were partitioned according to study design (randomized vs. nonrandomized), country in which the study was conducted (United States vs. other), study quality (0–2 vs. 3–5), menopausal status (pre vs. post), calcium supplementation, changes in dietary intake during the study, drugs that could affect BMD, and physical activity habits of subjects. For the femur site, we also examined changes in BMD with data partitioned according to the femoral neck, trochanter, intertrochanter, and Ward's triangle. We were unable to examine specific sites at the lumbar spine and radius because of insufficient data. Bootstrap resampling (5,000 iterations) was used to generate 95% confidence intervals around ES changes for all subgroups. Randomization tests (5,000 iterations) were used to generate probability values for between-group differences.[69] Randomization tests using 5,000 iterations can detect a probability as low as 0.002.[69]

Regression Analysis. For continuous variables, potential associations with ES changes in BMD were conducted using meta-regression procedures, calculated with each ES weighted by the reciprocal of its variance, according to procedures described by Hedges and Olkin.[62] This model yields a test of the significance of each predictor (Q_R) as well as a test of model specification (Q_E) which assesses whether systematic variation remains unexplained in the regression model. Thus, a statistically significant Q_R value means that the variables included in the regression are significantly related to the variable of interest, whereas a nonsignificant Q_E value means that the model is well specified. Continuous variables that were examined included percentage

of dropout (number of subjects who did not complete the study), age, height, initial as well as changes in body weight, body mass index, percentage of body fat and lean-body mass, changes in muscular strength, initial BMD, calcium intake, years postmenopausal, length and intensity of training, number of exercises performed, and compliance, defined as the percentage of exercise sessions attended by the subjects.

Secondary Outcomes. Secondary outcomes (changes in body weight, body mass index, percentage of body fat, and lean-body mass) were calculated as the difference (exercise minus control) of the changes (initial minus final) in these mean values. The original metric was used for all secondary outcomes. For those studies in which variance estimation was necessary, these were accomplished using the same procedures as those for estimating variances for BMD.[63] Fixed and random effects models were used following the same procedures as those previously described for BMD. Percentage of changes in muscular strength (one repetition maximum) were reported separately for exercise and control groups.

Unless otherwise noted, all results are reported as mean ± SD. The α level for statistical significance was set at $P < 0.05$. Values between 0.05 and 0.10 were considered as a trend toward statistical significance. Bonferroni adjustments were not made because of the increased risk of a type 2 error.

RESULTS

Study Characteristics

Thirty-one studies met the criteria for inclusion.[24–52, 59, 60] However, we were unable to include two studies[59, 60] because of the inability to obtain data necessary for the calculation of an ES. Thus, we had a 6% loss that met our inclusion criteria. One study[70] was excluded because it included some of the same subjects from another study that we included.[40] A general description of the 29 included studies is shown in Table 1 and the physical characteristics of the exercise and control group subjects are described in Table 2. The per person time to code each study once ranged from 0.58 to 4.67 hr (1.26 ± 0.79 hr). Study quality ranged from 1 to 4 (2 ± 1). The 29 included studies represented 94 ES (femur = 53, lumbar spine = 24, radius = 17) from 61 groups (32 exercise, 29 control). Twenty-three studies were published in journals,[25, 27–32, 34–38, 40, 42–50, 52] five were dissertations,[24, 26, 33, 39, 41] and one was a master's thesis.[51] Twenty studies were conducted in the United States,[24, 26–28, 33, 34, 36–39, 41–50] three in Finland,[30, 31, 52] two each in Austria[29, 40] and Canada,[25, 51] and one each in Australia[32] and France.[35] Percentage of dropout, defined as the number of subjects who did not complete the study, ranged from 0 to 63% in the exercise groups (28 ± 17%) and 0 to 69% in the control groups (17 ± 18%). Thus, pre and post measures of BMD were available for 572 subjects who served as exercisers and 551 subjects who served as controls. The minimum and maximum number of subjects in the exercise groups was 6 and 46 (18 ± 10), respectively, whereas the minimum and maximum number of subjects in the control groups was 7 and 42 (19 ± 10), respectively. For the 14 studies that reported information on race, 12 reported that all of the subjects were white,[26, 28, 33–36, 40, 43, 45–48] one study reported that the subjects were white and black,[42] and another reported that the subjects were white and Asian.[51] For the 18 studies that reported information on calcium supplementation during the study, eight studies reported that some subjects were taking supplements,[33, 36–38, 43, 46, 48, 51] seven reported that all of the subjects were taking supple ments,[24, 26–28, 34, 44, 49] and three reported that none of the subjects were taking supplements.[35, 39, 47] For the 23 studies that reported on whether subjects were taking any type of pharmacologic interventions that could affect BMD, 14 reported that none were taking any pharmacologic interventions,[26, 27, 32–37, 40, 42, 44, 46, 47, 51] eight reported that some were,[25, 28, 30, 31, 39, 43, 45, 48] and one study reported that all were.[38] Ten studies reported that none of the subjects smoked cigarettes,[25, 31, 33, 36, 39, 40, 44–47] whereas four reported that some subjects smoked.[28, 35, 48, 51] Two studies reported that some of the subjects consumed alcohol.[25, 48] Ten studies reported that none of the subjects had been previously active,[25, 26, 29, 31, 33, 34, 36, 39, 40, 43] eight reported that some were,[24, 28, 32, 35, 44, 48–50] and five reported that all were.[30, 37, 46, 51, 52] Five studies reported that none of the subjects had suffered previous fractures,[29, 39, 43, 46, 47] whereas three reported that some had.[33, 36, 40] Compliance, defined as the percentage of resistance training sessions that the exercise groups attended, ranged from 44% to 96% (79 ± 13%). Reliability for BMD assessment (coefficient of variation) ranged from approximately 0.6% to 4% at the femur, 0.6% to 5.0% at the lumbar spine, and 0.5% to 5% at the radius.

Primary Outomes

Initial BMD values for exercise and controls are shown in Table 3, whereas ES changes in BMD are shown in Table 4. BMD values were available for a total of 743 subjects at the femur (392 exercise, 351 control), 870 at the lumbar spine (450 exercise, 420 control), and 441 at the radius (219 exercise, 222 control). Because there was no statistically significant heterogeneity at any of the sites observed, a fixed-effects model was used for overall results at all three sites.

TABLE 2
Initial physical characteristics of subjects

Variable	*n*	Exercise (Mean ± SD)	*n*	Control (Mean ± SD)
Age (yr)	32	49.0 ± 17.9	29	47.7 ± 17.8
Height (cm)	27	163.2 ± 2.3	24	163.3 ± 2.8
Weight (kg)	30	63.5 ± 3.7	27	64.4 ± 3.3
BMI (kg/m^2)	28	23.9 ± 1.6	25	24.3 ± 1.5
Fat (%)	13	31.6 ± 5.8	12	31.7 ± 5.8
Lean mass (kg)	12	42.4 ± 3.3	11	42.4 ± 3.7
Postmenopausal (yr)	13	8.6 ± 4.7	12	8.5 ± 4.0
Calcium (mg)	16	926 ± 227	14	825 ± 114

n, number of groups reporting data; BMI, body mass index.

Proximal Femur. Small and statistically insignificant changes in BMD were observed at the femur site. These changes were equivalent to a 0.33% increase in the exercise groups and a 0.05% decrease in the control groups. No evidence of publication bias was observed ($r = 0.12$, $P = 0.26$). With each study deleted from the model once, ES changes in BMD at the femur ranged from a low of 0.02 ± 0.37 (95% Bootstrap Confidence Interval [BCI], −0.07–0.11) to a high of 0.09 ± 0.36 (95% BCI, 0.03–0.17). Approximately 90% of the 53 ESs were reported by the authors of the original studies as not being statistically significant.

Lumbar Spine. Small but statistically significant ES changes in BMD were found at the lumbar spine. These changes were equivalent to a 0.19% decrease in the exercise groups and a 1.45% decrease in the control groups. No evidence of publication bias was observed ($r = -0.08$, $P = 0.62$). With each study deleted from the model once, ES changes in BMD ranged from a low of 0.19 ± 0.37 (95% BCI, 0.09–0.33) to a high of 0.27 ± 0.36 (95% BCI, 0.14–0.41). Approximately 67% of the 24 ESs were reported by the authors of the original studies as not being statistically significant.

Radius. Small and statistically significant ES changes in BMD were observed at the radius. ES changes were equivalent to a 1.22% increase in BMD for the exercise groups and a 0.95% decrease in the control groups. No evidence of publication bias was observed ($r = 0.17$, $P = 0.38$). With each study deleted from the model once, ES changes in BMD at the radius ranged from a low of 0.19 ± 0.36 (95% BCI, 0.03–0.45) to a high of 0.33 ± 0.34 (95% BCI, 0.16–0.52). Approximately 65% of the 17 ESs were reported by the authors of the original studies as not being statistically significant.

Subgroup Analysis

Subgroup analyses for those variables in which there were statistically significant differences or trends for statistically significant differences between groups are shown in Table 5.

Femur. There was a trend for greater ES changes in BMD at the femur when studies were of higher vs. lower quality. Higher-quality studies yielded ES changes that were equivalent to a 1.03% increase in BMD in the exercise groups and a 0.16% increase in the control groups. Lower-quality studies yielded ES changes that were equivalent to a 0.21% increase in the exercise groups and a 0.09% decrease in the control groups. There was also a trend for greater ES changes in BMD at the femur when subjects were postmenopausal vs. premenopausal. For postmenopausal women,

TABLE 3
Initial BMD values

Variable	Studies (*n*)	Exercise Subjects (Mean ± SD)	Exercise Values (*n*)	Exercise (g/cm^2) (Mean ± SD)	Control Subjects (Mean ± SD)	Control Values (*n*)	Control (g/cm^2) (Mean ± SD)
Femur	22	18 ± 8	53	0.852 ± 0.197	16 ± 9	46	0.832 ± 0.178
Lumbar spine	23	20 ± 10	24	1.075 ± 0.115	18 ± 11	23	1.071 ± 0.121
Radius	10	22 ± 14	17	0.497 ± 0.153	22 ± 11	14	0.513 ± 0.160

BMD, bone mineral density; BMD data based on number of exercise and control values.

TABLE 4
BMD results

Variable	Studies (*n*)	Subjects (Mean ± SD)	ES (*n*)	ES (Mean ± SD)	BCI (95%)	Q (*P*)
Femur	22	34 ± 16	53	0.07 ± 0.36	−0.02to0.15	43.81 (0.78)
Lumbar spine	23	38 ± 20	24	0.24 ± 0.36	0.11to0.38[a]	20.68 (0.60)
Radius	10	44 ± 24	17	0.30 ± 0.33	0.13to0.48[a]	23.69 (0.10)

[a] Statistically significant.
BMD, bone mineral density; ES, effect size; BCI, Bootstrap Confidence Interval, Q (*P*), heterogeneity (probability for alpha).

ES changes in BMD were equivalent to a 0.40% increase in the exercise groups and a 0.21% decrease in the controls. For premenopausal women, ES changes were equivalent to a 0.26% increase in the exercise groups and a 0.13% increase in the control groups. No statistically significant between-group differences were found when data were partitioned according to study design, country in which the study was conducted, calcium supplementation, previous physical activity habits, type of BMD assessment, and different sites at which BMD was assessed. Insufficient data were available to examine differences in BMD at the femur when data were partitioned according to diet as well as drugs that could affect BMD.

Lumbar Spine. No statistically significant between-group differences were observed for ES changes at the lumbar spine when data were partitioned according to source of study, country in which the study was conducted, study design, menopausal status of subjects, calcium supplementation, previous physical activity, and type of BMD assessment. Insufficient data were available to examine between-group differences in BMD when data were partitioned according to study quality, drugs that could affect BMD, diet, and sites at which the lumbar spine BMD was assessed.

Radius. There was a trend for greater ES changes in BMD at the radius when studies were of higher vs. lower quality. Higher-quality studies yielded ES changes that were equivalent to a 0.82% increase in BMD in the exercise groups and a 1.87% decrease in the control groups. Lower-quality studies yielded ES changes that were equivalent to a 1.75% increase in BMD in the exercise groups and a 0.23% increase in the control groups. ES changes at the radius were also greater in postmenopausal vs. premenopausal women. For postmenopausal women, ES changes were equivalent to a 1.71% increase in BMD in the exercise groups and a 1.39% decrease in the control groups. For premenopausal women, ES changes were equivalent to a 0.17% increase in the exercisers and a 0.01% increase in the controls. No statistically significant differences

TABLE 5
Subgroup analyses

Variable	Studies (*n*)	Subjects (*n*)	ES (*n*)	ES (Mean ± SD)	BCI (95%)	Q_b (*P*)
Femur						
Study quality						
0–2	21	682	45	0.03 ± 0.37	−0.07–0.10	3.05 (0.08)[a]
3–5	1	61	8	0.24 ± 0.37	0.03–0.44	
Menopausal status						
Premenopausal	9	309	28	−0.01 ± 0.36	−0.16–0.09	2.34 (0.09)[a]
Postmenopausal	12	381	24	0.15 ± 0.38	0.03–0.28	
Radius						
Study quality						
0–2	7	296	8	−0.01 ± 0.38	−0.09–0.05	14.11 (0.001)[b]
3–5	3	145	9	0.56 ± 0.36	0.38–0.75	
Menopausal status						
Premenopausal	4	202	5	−0.02 ± 0.42	−0.13–0.05	9.99 (0.004)[b]
Postmenopausal	5	186	11	0.52 ± 0.36	0.33–0.71	

ES, effect size; BCI, Bootstrap Confidence Interval; Q_b, difference between groups.
[a] Trend for statistical significance when P ranges from ≥ 0.05 to ≤ 0.10; [b] Statistically significant when $P < 0.05$.
ES outcomes based on number of ESs.

were observed when data were partitioned according to source of study, country in which the study was conducted, study design, previous physical activity habits, and type of BMD assessment. Insufficient data were available to examine between-group differences in BMD when data were partitioned according to calcium supplementation, drugs that could affect BMD, diet, and different sites at which BMD of the radius was assessed.

Regression Analyses

Femur. The only significant predictor for ES changes in BMD at the femur was changes in the percentage of fat ($Q_R = 6.67$, $P = 0.03$; $Q_E = 14.32$, $P = 0.35$). Larger ES changes in BMD at the femur were observed among subjects with smaller changes in the percentage of fat. No other statistically significant associations were observed.

Lumbar Spine

No significant predictors were observed for ES changes in BMD at the lumbar spine.

Radius. The only significant predictor for ES changes in BMD at the radius was initial lean-body mass ($Q_R = 6.76$, $P = 0.009$; $Q_E = 9.26$, $P = 0.41$). Smaller ES changes in BMD at the radius were observed among subjects with higher initial levels of lean-body mass. Insufficient data were available to examine the relationship between ES changes in BMD and changes in the percentage of body fat and lean-body mass.

Secondary Outcomes

Statistically significant decreases were observed for the percentage of body fat ($-2 \pm 2\%$; 95% BCI, -3 to -1%), whereas there was a statistically significant increase in lean-body mass (2 ± 1 kg; 95% BCI, 1–2 kg). No statistically significant changes were observed for body weight or body mass index. There was a 40% increase in muscular strength in the exercise groups and a 6% increase in the control groups.

DISCUSSION

Implications for Practice

The overall results of this study suggest that across all groups of women included in this analysis, resistance training helps to preserve lumbar spine BMD. Resistance training also seems to increase and preserve BMD at the femur and radius sites in postmenopausal women. Furthermore, with the exception of changes in BMD at the proximal femur, these results were consistent after deletion of each study once from our models.

An interesting finding of this study is the fact that the largest effect on BMD occurred at the radius site in postmenopausal women. One possible reason for this may be the fact that most subjects included in these studies were able to ambulate. Consequently, they may have had greater daily loading placed on the lumbar spine and femur vs. the radius before participation in the studies. Therefore, there may have been an opportunity for resistance training to have a greater effect on BMD at the radius vs. the lumbar spine and femur. However, it may also be that the resistance training programs placed greater relative loads on the radius vs. the lumbar spine and femur sites. The larger changes observed in BMD at the femur when changes in the percentage of fat were smaller as well as the smaller changes at the radius when initial lean-body mass was higher are supportive of the fact that in general, women who weigh more place greater stress on their bones. Thus, heavier women may not experience the same improvements in BMD as leaner women.

Although it seems that postmenopausal women may have the most to gain from a program of resistance training, this form of intervention should almost always be encouraged across all age groups, especially because of other benefits that can be derived from participation in such activities. For example, in this investigation, we saw statistically significant improvements in body composition (decreases in the percentage of body fat and increases in lean-body mass). However, we believe that it is unrealistic to think that any optimal training program (resistance, exercises, sets, repetitions, length of rest intervals, total workload) will ever be developed for maximizing BMD. The best that can occur is some minimal levels to achieve the desired changes. However, even these recommendations are imprecise. For example, despite the various training protocols used in the studies included in this meta-analysis, the deletion of each study once from the analysis had little effect on the overall results. Thus, the best recommendation we can make at this time is to adhere to the general principles of specificity and overload when prescribing resistance training programs aimed at maintaining and/or improving BMD.[5]

Although it is encouraging that resistance training seems to have positive effects on BMD at the lumbar spine, femur, and radius, the clinical importance of such small effects is not known, especially as it relates to fracture risk. We are not aware of any randomized trial(s) that have proven that resistance training reduces the risk of fracture. However, it may be that other factors contribute to increases in bone strength and subsequent reductions in fracture risk. For example, a recent animal study[71] found that mechanical loading improves bone strength by reshaping the bone structure with no apparent increase in BMD. Thus, resistance training may have a similar effect in humans.

Because most of the studies included in this meta-analysis examined the efficacy (does the treatment

work?) of resistance training for enhancing BMD in women, the effectiveness (does the treatment work in the real world?) of such an intervention could be questioned. This may be especially important given the fact that in the United States only 16% of people between the ages of 18 and 64 yr report regular participation in progressive resistance exercise.[72] It may be that other forms of therapy (calcium and/or vitamin D supplementation, hormone replacement therapy, selective estrogen receptor modulators, bisphosphonates) not only have a greater impact on BMD, but they also reduce the risk of fracture. For example, a recent meta-analysis[73] examined over a 3-yr period the effects of 10 mg of alendronate on BMD in osteoporotic women between the ages of 42 and 85 yr. The authors reported increases in BMD of 8.8% at the spine, 7.8% at the trochanter, and 5.9% at the femoral neck. The estimated cumulative incidence of nonvertebral fractures after 3 yr was 12.6% in the placebo group and 9.0% in the alendronate-treated group. It was concluded that administration of alendronate reduces the risk of nonvertebral fractures in osteoporotic postmenopausal women. Given the former, resistance training in conjunction with other types of nonpharmacologic and/or pharmacologic therapy may be most appropriate, especially for those women with osteoporosis.

Implications for Research

One of the surprising findings of this study was the fact that changes in BMD were greater in studies of higher quality. It is generally believed that studies of higher quality yield less positive results than studies of lower quality. For example, a recent study,[74] using the same quality rating scale as ours, examined the impact of study quality on outcomes in placebo-controlled trials of homeopathy. These authors[74] concluded that studies of higher methodologic quality produced less positive results. However, it may be possible that trials with good designs reduce random variability and allow the intervention to produce a larger ES. This may have been the case with our investigation.

The fact that we included both randomized and nonrandomized controlled trials in our study could be questioned. It is generally felt that randomized trials yield results that are more conservative when compared with nonrandomized trials. However, because we did not find a statistically significant difference between any of our outcomes when the data were partitioned by study design, we felt it was appropriate to include both in our analysis.

Although it is important to conduct many statistical tests when performing a meta-analysis, some of our statistically significant results may have been the result of chance vs. any real effect. However, we believe that a greater risk existed of committing a type 2 error if Bonferroni adjustments were made to our data. Thus, our data were analyzed without any type of Bonferroni adjustments.

Although some may feel that the inclusion of dissertations and master's theses which have not been published as journal articles is inappropriate because they lack the same "rigor," we believe that it is critical, given appropriate resources, to include such because of the reported publication bias that has been shown to exist in the literature.[75, 76] For example, Stern and Simes[76] found that approximately 96% of selected psychology journals and 85% of selected medical journals published studies that yielded a statistically significant result. The inclusion of unpublished data represents a feeling that is shared by the majority of meta-analysts and methodologists, as a study by Cook and colleagues[77] has shown that approximately 80% feel that unpublished material such as dissertations and master's theses should definitely or probably be included in scientific overviews.

Despite the knowledge that studies can be more objectively evaluated using the meta-analytic vs. traditional, narrative approach, potential problems still exist. In general, the very nature of meta-analysis dictates that the meta-analysis itself inherits those limitations that exist in the literature. Therefore, the meta-analyst must point out these limitations and provide directions for future research. One of the common problems in meta-analysis is the issue of missing data for outcomes other than the primary ones of interest. For example, the fact that insufficient data were available to perform subgroup analysis on BMD at different lumbar and radius sites could have impacted our results. Although the inability to compare BMD at different lumbar and radius sites was more a function of a lack of sample size vs. the absence of reporting such information, additional studies directed at these sites would seem appropriate. In addition, we would suggest that future studies dealing with the effects of resistance training on BMD in women do a better job of assessing and reporting on the dietary habits of their subjects as well as the types of pharmacologic interventions that these subjects may be taking. Furthermore, because few studies included an assessment of the alcohol and calcium intake of the subjects, greater attention to these in the future seem warranted. It is also recommended that future studies include an evaluation of their data using both an analysis-by-protocol as well as an intention-to-treat approach. As a result, one may examine both the efficacy and effectiveness of resistance training for enhancing BMD in women. This will help provide clinicians with more meaningful information regarding the use of resistance training for enhancing BMD in women. Additional information regarding appropriate study design when examining the effects of exercise on BMD may be found in the excellent review of Snow

et al.[78] Finally, it would seem plausible to suggest that a need exists for a large randomized trial that examines the effect of resistance training on both BMD and fracture risk. However, a trial of this nature may never be successfully conducted.

In conclusion, the results of this meta-analysis suggest that resistance training has a positive effect on the BMD of all women at the lumbar spine, and in postmenopausal women at the femur and radius.

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Retrieval of Individual Patient Data for an Exercise Meta-Analysis

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The purpose of this study was to examine the feasibility of acquiring individual patient data (IPD) for a meta-analysis on the effects of exercise on bone mineral density in adults. We were able to obtain data from 29 (38.2%) of the 76 eligible studies. Binary multiple logistic regression analysis revealed a trend suggesting that authors of studies conducted in the United States were less likely to supply IPD when compared with authors who conducted studies in other countries (adjusted odds ratio, 0.324; 95% confidence interval, 0.104–1.004). Only 19% of authors from studies conducted in the United States vs. 52.9% of authors from other countries provided us with IPD. We conclude that we received a low response rate in the acquisition of IPD for a meta-analysis dealing with the effects of exercise on bone mineral density in adults. The use of summary means vs. IPD may be more appropriate for studies of this nature. (Am J Med Sports. 2002;4:350–354)

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The use of meta-analysis is becoming increasingly common in the exercise training and physical activity literature. A recent MEDLINE search by one of the authors (KSK) found that the number of citations listed using the keywords "exercise and meta-analysis" has increased from two between the years 1980–1985 to 121 between the years 1995–2000 (unpublished results). To the best of our knowledge, all meta-analyses on this topic conducted to date have derived their results from the aggregation of summary data provided in the studies. An alternative approach is the retrieval of individual patient data (IPD) from study authors.

One of the major advantages of using IPD in a meta-analysis is the potential for increased statistic power as well as a more thorough examination of potential covariates.[1–3] Therefore, the use of IPD may be especially appropriate, since many meta-analyses include a small number of studies, thus limiting the interpretation and application of the findings.

One of the potential disadvantages with the retrieval of IPD is the inability to obtain IPD from studies that meet one's predefined inclusion criteria. This results in a form of bias known as retrieval bias.[2] In addition, meta-analyses of IPD are traditionally more expensive and labor-intensive than meta-analyses using summary means. Consequently, the use of summary data from individual studies may be preferable.

We have previously published meta-analytic work dealing with the effects of exercise on bone mineral density (BMD) in adult humans.[4–8] While our previous work has resulted in some noteworthy findings, these meta-analyses were based on the aggregation of summary data from individual studies. Unfortunately, we were limited in our ability to perform subgroup analyses because of a lack of information. The ability to examine potential factors associated with exercise-induced changes in BMD is important for deriving a better understanding of the true relationship between exercise and BMD. Since the acquisition of IPD could lead to a more accurate determination of the role of exercise on BMD, we sought such data from study

authors. Thus, the purpose of this paper is to report on the level of success of acquiring IPD dealing with the effects of exercise on BMD in adult humans.

Methods

ACQUISITION OF IPD DATA. The acquisition of IPD was conducted according to the general guidelines of Friedenreich.[9] For this study, references for IPD were derived from a database that contained 76 studies that met our previously defined meta-analytic inclusion criteria on the effects of exercise on BMD in adults (references available on request). Prior to sending out our request for IPD, a cover letter and IPD request sheet were developed, reviewed, revised, and approved by the three authors. We then sent, via postal mail, a copy of the cover letter and an IPD data acquisition form to the corresponding authors of the 76 studies. A follow-up request, approximately 5 weeks later, was sent to all authors who did not respond to our initial request. If the corresponding author referred us to one of the coauthors, contact was made with that author in an attempt to retrieve IPD. The first request contained no deadline date for the receipt of IPD. However, the second request included a deadline date of approximately 4 weeks from the date of mailing for the receipt of IPD. This deadline was extended for those authors who contacted us to request additional time to provide us with IPD. Some individual patient data were already available from five of the original studies in our database (i.e., from the published tables). However, requests were also sent to the corresponding authors of these studies in the event that additional IPD data might be provided. All authors who supplied IPD were mailed a check for US $40 to help cover incurred costs. We were limited to this amount of money because of budget limitations. Prior to the start of this study, approval was obtained by the Institutional Review Board at Massachusetts General Hospital.

STATISTICAL ANALYSIS. Descriptive statistics (frequencies, percentages, ranges, means, and standard deviations) were used to report overall results. Binary multiple logistic regression was used to examine potential predictors for whether IPD were finally sent to us or not. Predictors in the model included gender of author contacted, source of publication (journal vs. other), country in which the study was conducted (United States vs. other), and year of publication. The likelihood ratio statistic and Hosmer and Lemeshow test were used to identify whether the model adequately fit the data. The Nagelkerke *R*-squared statistic was used to identify the amount of variance accounted for by the predictor variables.[10] The Nagelkerke *R*-squared statistic is an adjusted version of the Cox and Snell *R*-squared. This adjustment was necessary because the Cox and Snell *R*-squared statistic has a value less than 1 even for a perfect model. Significance of regression coefficients for individual predictor variables was examined using the Wald statistic. In addition, odds ratios and 95% confidence intervals (CI), adjusted for other variables in the model, were used to examine the significance of individual predictor variables. Comparison of models with and without interactions was examined using the G test, which compares the log likelihoods between two models.

For comparative purposes, BMD results were calculated using the standardized difference effect size (ES) estimated from the summary data reported in the studies and corrected for small sample bias.[11] We were unable to use the original metric because of missing data. The standardized difference ES was calculated by taking the difference in BMD between the exercise and control groups and dividing by the pooled standard deviation of the exercise and control groups.[11] For studies that did not supply these data, the ES was calculated from other reported statistics by previously developed methods.[12] In general, an ES of 0.20 is considered a small effect, 0.50 a moderate effect, and 0.80 a large effect.[13] An ES of 0.20 for example, means that the exercise group differed from the control group by only two tenths of a standard deviation in favor of the exercise group. We then compared ES differences between those studies that did and did not provide IPD, using an analysis of variance-like random effects model developed for meta-analytic research.[11] This was accomplished by examining the between (Q_b) and within (Q_w) group differences for the ESs and their variances from each group. In addition, for those studies that supplied IPD, this approach was used to examine whether any statistically significant or clinically important differences existed between calculations of ESs from IPD and summary data reported in the studies.

The alpha level for a type I error was set at $p \leq 0.05$. Ninety-five percent CIs that did not cross zero were considered statistically significant. Trends were defined as values >0.05 but ≤ 0.10.[14,15]

Results

DESCRIPTION OF RESPONSES. Of the 76 requests mailed out, 41 (53.9%) authors responded, 33 (43.4%) did not respond at all, and two (2.6%) were returned to us because of undeliverable/invalid addresses. The reasons given by those authors who responded to our request but never supplied IPD data are shown in Table I. Of the 41 who did respond, 26

of the 74 total, or 35.1%, provided us with IPD data. Of the 26 authors who provided IPD data, 22 (84.6%) sent their data as an attachment via electronic mail (our suggested preference), while two each sent data via either postal mail (7.7%) or facsimile (7.7%). The time taken from the date initial letters of request were mailed to the date that data were received ranged from 14–89 days ($\overline{X}$ ±SD = 50±23 days). Of the 22 authors who provided IPD via electronic mail, 15 (68.2%) included their data as a Microsoft Excel attachment (our suggested preference), while the remaining seven (31.8%) provided data as an SPSS file. Individual patient data provided from one author (for one study) could not be used because of missing data for BMD and our inability to contact this author at follow-up. Individual patient data from another author (for one study) was also excluded because it was a subset of data from another study already included in our database. Thus, we received usable IPD data for 24 of 76 studies (31.6%) for which data were requested. In addition, we already had in our possession IPD data from a total of five (6.6%) other studies. This left us with 29 studies (38.2%) for future IPD level analysis.

LOGISTIC REGRESSION ANALYSIS. The results of our binary multiple logistic regression analysis are shown in Table II. Approximately 21% of the variance was accounted for by the predictor variables (R^2_{adj}=0.207). Both the likelihood ratio statistic (χ^2=12.046; p=0.017) and Hosmer and Lemeshow test (χ^2=4.660; p=0.793) demonstrated that the model adequately fit the data. There was a trend for country where the study was conducted (United States vs. other) to be a predictor of whether or not IPD were provided, suggesting that authors of studies conducted in the United States were less likely to supply IPD when compared with authors who conducted studies in other countries. Only 19.0% of authors from the United States, vs. 52.9% of authors from other countries, provided us with IPD. No other variables were significant predictors for whether IPD would be provided.

Since there was a statistically significant association between country and year of publication (r=0.330; p=0.004), we compared our original model with a second model that included the interaction between country and year of publication. No statistically significant difference was found between the two models (G=0.464; p=0.496).

ES COMPARISONS. No statistically significant or clinically important differences were found in BMD between those studies that provided IPD vs. those that did not (IPD provided: $\overline{X}$±SD=0.134±0.364; 95% CI=0.069–0.198; IPD not provided: $\overline{X}$±SD=0.195±0.387; 95% CI=0.143–0.247; Q_b=2.126; p=0.145). In addition, for those studies that supplied IPD, no statistically significant or clinically important differences were found between calculations of ES from IPD and summary data reported in the studies (calculations from IPD: $\overline{X}$±SD=0.179±0.413; 95% CI=0.106–0.252; calculations summary data: $\overline{X}$±SD=0.134±0.364, 95% CI=0.069–0.198; Q_b=0.664; p=0.415).

Discussion

While the acquisition of IPD for meta-analytic purposes can lead to increased statistical power and a more thorough examination of potential covariates, the results of our investigation suggest that obtaining such data from authors of intervention studies dealing with the effects of exercise training on BMD in adults is difficult (31.6% of authors contacted provided IPD). This, coupled with the increased costs associated with the retrieval of IPD,[1] as well as the fact that we found no differences in BMD between studies that provided IPD vs. those that did not, suggests that the use of summary data from the actual studies may be more appropriate for examining the effects

Table I. Responses of Investigators Who Responded to the Authors' Request but Never Supplied IPD

No. of Authors	Results/Responses
6	Data no longer available
2	Data no longer available because of a change in computer systems
3	Corresponding author did not have data; referred us to another author who did not respond and/or did not send data
1	Expressed an interest in providing data but never provided such
1	Did not have time to track down data
1	Not willing to supply data until published in a refereed journal (original source was a dissertation)
1	Not willing to supply data because meta-analysis is inappropriate for exercise and bone mineral density studies

Table II. Results of Multiple Logistic Regression Analysis (n=74)

VARIABLE	B	SE	*DF*	SIGNIFICANCE	EXP(B)	95% CI
Constant	−275.443	190.997	1	0.149	0.000	NA
Country	−1.128	0.577	1	0.051*	0.324	0.104–1.004*
Gender	0.246	0.544	1	0.652	1.279	0.440–3.716
Source	0.614	1.179	1	0.602	1.848	0.183–18.627
Year	0.138	0.096	1	0.146	1.150	0.951–1.385

B=regression coefficients for the logistic regression; SE=standard error of the regression coefficients; *df*=degrees of freedom; Exp(B)=odds ratio, adjusted for independent variables; 95% CI=95% confidence interval for the odds ratio; *trend for statistical significance

of exercise training on BMD in adults. In addition, the inability to acquire IPD results in greater information bias, thus limiting the interpretation of findings from such studies. Thus, the use of summary means vs. IPD when conducting a meta-analysis on the effects of exercise training on BMD in humans should result in a more accurate as well as cost- and time-effective investigation. This is important because it would allow those with limited resources to conduct studies of this nature. Furthermore, given the proliferation of information in the health care field, a continued need for meta-analysis will exist.

We are not aware of anyone else who has attempted to retrieve IPD for an exercise-related meta-analysis. While the retrieval of IPD for meta-analyses may be problematic across all fields, including exercise, our results suggest that it may be especially problematic for those individuals interested in conducting IPD meta-analyses of exercise and bone studies. For example, Arnot et al.[16] were able to retrieve IPD from five of seven trials (71.4%) dealing with the effects of preoperative radiation therapy in esophageal carcinoma. Another meta-analysis reported the retrieval of IPD from 39 of 63 studies (61.9%) that met their inclusion criteria on the topic of breast cancer and hormone replacement therapy.[17] This compares to approximately 32% in our study.

One of the surprising findings of this study was the trend for more authors from studies conducted in countries other than the United States to provide us with IPD. While purely speculative, it may be that authors of studies conducted in the United States were less likely to provide us with IPD because they did not want to take the time to retrieve such information. This may be especially true given the small amount of money (US $40) we provided them for the retrieval of such. Unfortunately, we were not able to provide more money because of budget limitations. Alternatively, $40 to researchers in some foreign countries may represent a significant amount of money, thus resulting in a greater willingness to supply IPD.

Another possible reason for the low response rate from studies conducted in the United States may have to do with the investigators' concerns about protecting their data because of the potential misuse of such. For example, the strict guidelines that are enforced by the vast majority of university and hospital institutional review boards in the United States surrounding issues such as subject confidentiality may have precluded authors from supplying us with IPD. However, we believe that concerns about approbation from institutional review boards should not be an issue, as researchers should have data storage systems that protect the confidentiality of patients. Consequently, the sharing of IPD should not be a problem. Researchers who informed us that the data are "no longer available" were troubling in that the failure to sustain IPD in a manner that allows for verification of an analysis might be considered an ethical issue. Alternatively, this may be an issue of nothing more than selfishness on the part of some investigators. Since cooperation and trust are part of the foundation of science, we believe that any acts of selfishness on the part of investigators should be discouraged.

Since our investigation was limited to studies dealing with the effects of exercise on BMD, it may be inappropriate to generalize our results to other exercise meta-analyses. This, coupled with the fact that we are not aware of any other work in the meta-analytic field that has focused on predictors for retrieval of IPD, would lead us to suggest that future research in the meta-analytic field in general, and the exercise and meta-analysis field in particular, focus on this area. This may be especially important, since only 21% of the variance was accounted for in our logistic regression model. Thus, it appears that there may be other unknown factors, or combinations of factors, surrounding the retrieval of IPD.

In conclusion, the results of our study suggest a low response rate in acquiring IPD for a meta-analysis dealing with the effects of exercise training on BMD in adults, and show that success appears to be greater when IPD are requested for studies conducted in countries other than the United States. Given the relatively low response rate, and thus increased bias, the use of summary data may be more appropriate for examining the effects of exercise training on BMD in adults. ■

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Aerobic Exercise and Regional Bone Density in Women: A Meta-Analysis of Controlled Trials

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In this study the meta-analytic approach was used to examine the effects of aerobic exercise on regional bone mineral density at the lumbar spine, femur, and radius in women. Twenty-four studies representing 58 groups (31 exercise, 27 control) and 1029 subjects (517 exercise, 512 control) met the criteria for inclusion. Using a random-effects model, small but statistically significant effect size changes in bone mineral density were observed at the lumbar spine ($\bar{X}$ ±SD=0.33±0.49; 95% confidence interval=0.16–0.50) and femur ($\bar{X}$ ±SD=0.25±0.35; 95% confidence interval=0.14–0.35). Changes in lumbar spine bone mineral density were equivalent to a 0.37% increase in the exercise groups and a 1.87% decrease in the control groups. For the femur, changes were equivalent to a 1.37% increase in the exercise groups and a 0.58% decrease in the control groups. No statistically significant changes were observed at the radius ($\bar{X}$ ±SD=0.10±0.45; 95% confidence interval=−0.20 to 0.41). The overall results of this study suggest that aerobic exercise has a small but positive effect on bone mineral density at the lumbar spine and femur in women. (Am J Med Sports. 2002; 4:427–433, 452)

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Osteoporosis, defined as abnormally low bone mass, is a major public health problem in the United States, as well as other countries. In 1996, it was estimated that approximately 23 million women in the United States had osteoporosis or were at risk for developing the disease.[1] By the year 2015 this figure is expected to increase to approximately 35 million.[2] It is well established that low bone mineral density (BMD) is associated with increased fracture risk. The health care costs associated with osteoporotic fractures has been reported to exceed $13.8 billion annually.[3] Given the health and economic costs associated with osteoporosis, a need exists for appropriate nonpharmacologic and pharmacologic interventions for dealing with this disease. One such nonpharmacologic intervention may be aerobic exercise,[4] a low-cost intervention that is available to most of the general public.

We have previously reported that aerobic exercise might help to maintain and/or increase BMD in postmenopausal women but that additional studies were needed before any firm conclusions could be reached.[5–7] Since the time of these published meta-analyses, a number of additional studies have been conducted and/or located. It is critical that up-to-date meta-analyses be performed in order to provide the most recent information possible on the state of knowledge regarding the topic of interest. Given the health care consequences of low BMD, it is important to understand the role that aerobic exercise may play as a nonpharmacologic intervention for enhancing and/or maintaining BMD in women. Thus, we used the meta-analytic approach to examine the effects of aerobic exercise on regional BMD at the lumbar spine, femur, and radius in women.

Methods

DATA SOURCES. Computerized literature searches of articles indexed between January, 1966 and December, 1998 were performed using MEDLINE, Embase, Current Contents, Sport Discus, and Dissertation Abstracts International Databases. The key words used in this literature search were "exercise" and "bone."

While this broad approach to searching the literature will result in the retrieval of a greater number of articles to review, it should decrease the number of studies missed when a more narrow and focused search is conducted. In addition to computerized literature searches, the reference lists from both original and review articles were examined in order to identify any studies that had not been previously identified and that appeared to contain information that may have met our inclusion criteria. Finally, three experts on exercise and bone density (Dr. David Nichols, Dr. Charlotte Sanborn, and Dr. Christine Snow) reviewed our reference list for thoroughness and completeness.

STUDY SELECTION. The inclusion criteria for this study were as follows: 1) trials were randomized or nonrandomized trials and included a comparative nonexercise group; 2) aerobic exercise was the only intervention; 3) subjects were adult female humans (mean age, 18 years or older); 4) studies were reported as journal articles, dissertations, and master's theses published in the English language literature; 5) studies were published and indexed between January, 1966 and December, 1998; 6) BMD (relative value of bone mineral per measured bone area) was assessed at the femur, lumbar spine, or radius; and 7) training studies which lasted a minimum of 16 weeks. Only studies that met the above criteria were included in our analysis. Thus, for example, if BMD was also assessed in women performing progressive resistance exercise as the primary training modality, we did not include this information since it did not meet our inclusion criteria. Because dissertations and master's theses may eventually become full-length journal articles, we cross-referenced between the two in order to avoid duplication. We did not include abstracts and conference papers from national meetings because of the paucity of data provided as well as the inability to obtain complete data from the authors. Studies published in foreign language journals were also not included because of the potential error in the translation and interpretation of findings. Studies that met our inclusion criteria were also examined to ensure that the same subjects were not included in more than one study.[8] For studies that met our inclusion criteria but did not provide appropriate information on changes in BMD, personal contact was made with the authors in an attempt to retrieve such information.

DATA ABSTRACTION. Coding sheets that could hold 242 items per study were developed and utilized in this study. In order to avoid inter-coder bias, all data were independently abstracted by both authors. The authors then met and reviewed every data point for accuracy and consistency. Disagreements were resolved by consensus. The major categories of variables coded included study characteristics, physical characteristics of subjects, and primary and secondary outcomes.

STATISTICAL ANALYSIS. ***Primary Outcomes.*** The primary outcomes in this study were changes in BMD at the lumbar spine, femur, and radius, calculated using the standardized difference effect size (ES) approach. This was accomplished by subtracting the change outcome in the exercise group from the change outcome in the control group, then dividing this difference by the pooled standard deviation of the exercise and control groups.[9] This measure provides one with a statistic similar to a *z* score. In general, an ES of 0.20 is considered a small effect, 0.50 a moderate effect, and 0.80 a large effect.[10] An ES of 0.30 for example, means that the exercise group differed from the control group by three-tenths of a standard deviation in favor of the exercise group. Using a *z* score table, this means that the exercise group would do better than approximately 62% of the control group. We used this approach vs. the original metric because of the various ways in which the authors reported data on changes in BMD and because we also wanted to maximize the number of studies and outcomes that could be included in our analysis. All ESs were then corrected for small-sample bias.[9] For studies that did not report change outcome variances, these were estimated using previously developed methods.[11] T-distribution 95% confidence intervals (CI) were calculated for all outcomes. If the 95% CI included zero (0.00), it was concluded that there was no statistically significant effect of exercise on BMD. A random-effects model was used for all analyses.[9]

Heterogeneity of ESs was examined using the Q statistic.[9] For studies that included multiple outcomes because of more than one group, net changes were initially treated as independent data points. However, in order to examine the influence (sensitivity) of each study on the overall results, analyses were performed with each study deleted from the model for ES changes at the lumbar spine, femur, and radius. Publication bias (the tendency for journals and/or authors to publish studies that yield statistically significant results) was examined using a funnel plot.[12] This was accomplished by plotting the sample size on the vertical axis and ES changes in BMD on the horizontal axis. Usually, smaller studies tend to disperse at the bottom of the funnel while larger studies tend to congregate at the top. A gap at the bottom of the funnel on the left side indicates that small studies yielding null or negative results may be missing. Study quality was assessed using a three-item questionnaire designed to assess bias—specifically, randomization, blinding, and withdrawals/dropouts.[13] The number of points possible ranged from a low of 0 to a high of 5. All

questions were designed to elicit yes (1 point) or no (0 points) responses. The questionnaire, which took less than 10 minutes per study, has been shown to be both valid (face validity) and reliable (researcher inter-rater agreement: r=0.77; 95% CI=0.60–0.86).[13]

Subgroup Analyses. Subgroup analyses for ES changes at the lumbar spine and femur were performed using analysis of variance (ANOVA)-like procedures for meta-analysis.[9] These procedures provide statistics for both within (Q_w)- and between (Q_b)-group differences. A random-effects model was used for all analyses. Subgroup analyses were performed for: ES changes at the lumbar spine and femur according to type of publication (journal vs. dissertation); country in which the study was conducted (United States vs. other); study design (randomized vs. nonrandomized, controlled trial); whether subjects were postmenopausal; whether subjects were taking calcium supplementation; type of BMD assessment (dual-energy x-ray absorptiometry, dual photon absorptiometry, quantitative computed tomography); and higher vs. lower impact activity. Higher impact activities included exercises such as running, jumping, and aerobic dancing with both feet off the ground, while lower impact activities included exercises such as walking and low impact aerobic dancing with both feet on the ground. ES changes in BMD at the femur were also examined when data were partitioned according to whether drugs were taken that could enhance BMD, cigarette smoking, diet, previous physical activity, and the specific site of BMD assessment (femoral neck, trochanter, Ward's triangle, intertrochanter). Insufficient data were provided to examine ES changes in BMD at the lumbar spine according to whether drugs were taken that could enhance BMD, cigarette smoking, diet, previous physical activity, and the specific site at which BMD was assessed. For both the lumbar spine and femur, insufficient data were provided to examine changes in BMD when partitioned according to alcohol consumption and previous fractures. We were unable to partition the results according to training modality because of the variety of activities in which the subjects participated. We did not perform subgroup analysis for changes in BMD at the radius because of the small sample size. In addition, we were not able to examine differences between the radius and other sites at the forearm (for example, the ulna) because of insufficient data.

Regression Analysis. The potential associations between ES changes in BMD at the lumber spine and femur were conducted using simple weighted least-squares regression, according to procedures developed by Hedges and Olkin.[9] Variables included study quality, percent dropout, initial BMD, age, height, initial body weight, changes in body weight, initial body mass index, changes in body mass index, initial percent fat, changes in percent fat, initial lean body mass, changes in lean body mass, initial maximum oxygen consumption ($mL/kg^{-1}/min^{-1}$), changes in maximum oxygen consumption ($mL/kg^{-1}/min^{-1}$), years past menopause, initial calcium intake, changes in calcium intake, reliability of BMD measurements, length, frequency, intensity, and duration of training, total minutes of training (length × frequency × duration), and compliance, defined as the percentage of exercise sessions attended. Insufficient data were available to examine ES changes in BMD and resting heart rate. We did not conduct regression analyses for ES changes in BMD at the radius because of the small sample size. We were unable to conduct any type of multiple regression analyses because of missing data for different sets of variables.

Secondary Outcomes. Secondary outcomes (changes in body weight, body mass index, percent body fat, lean body mass, maximum oxygen consumption, resting heart rate, and calcium intake) were calculated as the difference (exercise minus control) of the changes (initial minus final) in these mean values. With the exception of the use of the original metric vs. standardized difference approach, changes in secondary outcomes were examined using the same procedures as those for BMD.

An independent t test (2-tailed) was used to compare differences in study quality between journals and dissertations. Unless otherwise noted, all results are reported as $\bar{X} \pm SD$. The alpha level for statistical significance was set at $p \leq 0.05$.

Results

STUDY CHARACTERISTICS. Twenty-seven studies met the criteria for inclusion[14–40]; however, we were unable to retrieve necessary data from three studies.[15,27,28] This resulted in a loss of approximately 11%. Thus, 24 studies representing 31 exercise and 27 control groups (some studies had more than one group) were included in our final analysis.[14,16–26,29–40] From these 24 studies, 31 effect sizes were generated for the lumbar spine, 42 for the femur, and 11 for the radius. Twenty-two of the studies were published in refereed journals[14,17–26,29,31–40] while the other two were dissertations.[16,30] Thirteen studies were conducted in the United States,[14,16,19,20,22,26,30,31,33,34,37–39] three each in Australia[18,35,36] and the United Kingdom,[17,21,32] two each in Finland[24,25] and Japan,[23,40] and one in China.[29] Thirteen of the studies were randomized, controlled trials,[16,17,21–25,29,31,32,35,36,39] while 11 were nonrandomized, controlled trials.[14,18–20,26,30,33,34,37,38,40] Study quality ranged from 0

to 5 ($\bar{X}$±SD=1.75±1.51). There was no statistically significant difference in study quality between studies published in journals and dissertations (p=0.65). A total of 1029 subjects (517 exercise, 512 control) completed pre- and post-assessments of BMD. The average number of subjects ranged from five to 49 in the exercise groups ($\bar{X}$±SD=17±12) and from four to 48 in the control groups ($\bar{X}$±SD=19±15). The percent dropout, defined as the percentage of subjects who did not complete the study, ranged from 0%–63% in the exercise groups ($\bar{X}$±SD=20%±16%) and from 0%–43% in the control groups ($\bar{X}$±SD=10%±11%).

SUBJECT CHARACTERISTICS. A description of the subject characteristics is shown in Table I. In six studies, all of the subjects were white[14,22,30,31,33,36]; in one study, all subjects with the exception of one (a black person) were white[20]; in one study, all subjects were Chinese[29]; and in one study, all subjects were Japanese.[40] In 19 studies, all subjects were postmenopausal[14,17–23,26,29–33,35–38,40]; in two studies, only some subjects were postmenopausal[25,34]; and in three studies, no subjects were postmenopausal.[16,24,39] In 14 studies, no subjects were taking any type of hormone replacement during the study[14,17–19,23, 30–36,38,40] and in six studies, some of the subjects were taking some type of hormone replacement therapy.[20–22,24,25,37] One study had two separate groups of subjects in which one group took some type hormone replacement therapy while the other did not.[26] In nine studies, all subjects were taking some type of calcium supplementation during the study[16,20,26,31–33,35,37,39]; in five studies, no subjects were taking any type of calcium supplementation[19,22,23,36,40]; and in two studies, some of the subjects took some type of calcium supplementation.[21,30] Another study had two separate groups of subjects, one who took some type of calcium supplementation and another who did not.[29] In one other study, all of the subjects in the control group took some type of calcium supplementation, while some in the exercise group did so.[14] In eight studies, food intake did not change during the study[14,17,19,22,24,26,32,38] and in one study, it did.[33] In six studies, none of the subjects smoked cigarettes[24–26,30,36,38] and in four studies, some of the subjects smoked.[17,19,21,37] In one study, none of the subjects in the control group smoked but some of the subjects in one of the two exercise groups smoked.[31] In another study, some of the subjects in the exercise group smoked but no subjects in the control group did.[18] In two studies, some subjects consumed alcohol during the study.[18,32] In two studies, no subjects had previous fractures,[29,38] while in another study, subjects did have previous fractures.[21] In 13 studies, none of the subjects had been active prior to taking part in the study[14,17,20, 22,24–26,30,31,33,37,38,40] and in six studies, some of the subjects had been previously active.[16,19,21,35,36,39] In one study, no subjects in the control group had been active prior to taking part in the study but subjects in the exercise group had been previously active.[34]

Table I. Subject Characteristics

VARIABLE	N	EXERCISE ($\bar{X}$±SD)	N	CONTROL ($\bar{X}$±SD)
Age (years)	31	57.9±12.7	27	58.2±13.2
Height (cm)	22	160.7±4.3	19	161.5±4.4
Weight (kg)	25	64.7±6.6	21	64.2±6.4
BMI (kg/m^2)	24	24.9±1.9	21	24.6±1.9
Fat (%)	13	38.2±4.8	10	37.9±6.5
Lean mass (kg)	13	41.2±3.5	10	39.8±2.8
Initial Vo_{2max} (mL/kg^{-1}min^{-1})	16	23.4±4.2	11	23.9±5.0
Initial RHR (bpm)	4	76.7±3.7	2	74.15±4.5
Postmenopausal (years)	22	10.0±5.4	18	11.7±5.8
Calcium (mg)	19	934±340	16	938±344

N=number of groups reporting mean data; BMI=body mass index; Vo_{2max}=maximal oxygen consumption; RHR=resting heart rate; bpm=beats per minute.

BONE DENSITY ASSESSMENT CHARACTERISTICS. Twelve studies assessed BMD at the lumbar spine using dual-energy x-ray absorptiometry (DEXA),[16,17, 21,23–26,29,35,38–40] seven studies used dual-photon absorptiometry (DPA),[14,18,20,22,30,31,34] and two used quantitative computed tomography (QCT).[19,32] One other study used both DPA and QCT to assess BMD at the lumber spine.[33] For studies that included such data, the vast majority reported the assessment of BMD at the L2–L4 sites.[16,17,20,22–25,29–31,34,38,39] Three studies reported the assessment of BMD at the L1–L4 sites,[14,35,40] one at the L1–L2 sites,[19] and another at the L1–L3 and L2–L4 sites.[33] Between-study mean reliability (coefficient of variation) of BMD assessment at the lumber spine ranged from 0.4%–3%. Ten studies used DEXA to assess BMD at the femur,[16,17,21, 24–26,29,35,38,39] while another five used DPA.[14,18,30,33,34] Fifteen studies included assessment of BMD at the femoral neck,[14,16–18,21,24–26,29,30,33–35,38,39] seven at Ward's triangle,[16,18,26,29,34,38,39] eight at the trochanter,[16,18,24,26,34,35,38,39] and two at the intertrochanter.[29,35] One study involved BMD assessment at the distal femur,[24] and another involved assessment of the total femur.[35] The mean between-study reliability (coefficient of variation) for BMD assessment at the femur ranged from 0.5%–4.4%. In eight studies, BMD was assessed at the forearm[24–26,30,33,34,36,37]; however, we were unable to identify whether one of the studies assessed BMD at the radius.[36] Four studies used single-photon

absorptiometry (SPA) to assess BMD at the radius,[30,33,34,37] while three used DEXA.[24–26] The mean between-study reliability (coefficient of variation) ranged from 0.5%–5.0%.

TRAINING PROGRAM CHARACTERISTICS. A description of the training program characteristics is shown in Table II. Overall, the activity most commonly included in these exercise interventions was walking. Specifically, five studies limited the training modality to primarily walking,[17,19,21,23,33] two to jogging,[16,39] and two to a combination of walking and jogging.[31,38] Two other studies had subjects participate primarily in aerobic dancing,[32,34] while another two employed walking[35,36] or aerobic dancing[18,22] as well as other activities. One study limited participants' exercise to stair stepping and other miscellaneous activities,[29] while another limited exercise to stationary cycling.[14] Two other studies had participants take part in a combination of walking, jogging, cycling, stair stepping, and other activities[20,25]; one had subjects perform walking, jogging, and stair stepping[26]; and another had subjects walk, swim, and perform other various activities.[40] One study had subjects perform aerobic dancing, stair stepping, and other assorted activities,[24] while another had subjects perform a variety of different but unspecified activities.[37] Finally, one study had one group of subjects who walked and another group who swam.[30]

PRIMARY OUTCOMES. *Lumbar Spine.* The overall results for ES changes in lumbar spine BMD are shown in Table III. As can be seen, small but statistically significant ES changes in lumber spine BMD were observed. These changes were equivalent to a 0.37% increase in the exercise groups and a 1.87% decrease in the control groups. No statistically significant heterogeneity was found for changes in lumbar spine BMD. Funnel plot analysis was suggestive of publication bias. With each study deleted from the model once, ES changes in BMD ranged from a low of 0.27±0.42 (95% CI=0.12–0.44) to a high of 0.36±0.48 (95% CI=0.18–0.54).

Femur. The overall results for ES changes in BMD at the femur are shown in Table III. As can be seen, small but statistically significant changes in BMD at the femur were observed. These changes were equivalent to a 1.37% increase in the exercise groups and a 0.58% decrease in the control groups. No statistically significant heterogeneity was found for changes in BMD at the femur. Funnel plot analysis was suggestive of publication bias. With each study deleted from the model once, ES changes in BMD at the femur ranged from a low of 0.21±0.34 (95% CI=0.10–0.32) to a high of 0.26±0.38 (95% CI=0.14–0.38).

Table II. Training Program Characteristics

VARIABLE	N	($\bar{X}$ ±SD)
Length (weeks)	31	53±23
Frequency (days/week)	28	3±1
Intensity (% Vo_{2max})	7	75±8
Duration (min/session)	22	33±11
Total min*	22	5046±3159
Compliance (%)	21	83±12

N=number of groups reporting mean data; Vo_{2max}=maximal oxygen consumption; *total minutes calculated as the product of length, frequency, and duration.

Radius. The overall results for ES changes in BMD at the radius are shown in Table III. As can be seen, changes in BMD at the radius were not statistically significant. ES changes were equivalent to a 0.08% decrease in BMD for the exercise groups and a 0.75% decrease in the control groups. No statistically significant heterogeneity was found for changes in BMD at the radius. Funnel plot analysis was not suggestive of publication bias. With each study deleted from the model once, ES changes in BMD at the radius ranged from a low of 0.02±0.37 (95% CI=−0.25 to 0.28) to a high of 0.17±0.42 (95% CI=−0.13 to 0.48).

Subgroup and Regression Analysis. Greater ES changes in BMD at the femur were observed for those subjects who received some type of calcium supplementation ($\bar{X}$ ±SD, calcium supplementation=0.33±0.42; no calcium supplementation, −0.24±0.44; Q_b=4.55; p=0.03). None of the other subgroup analyses at the lumber spine and femur were statistically significant or clinically important.

SECONDARY OUTCOMES. A statistically significant increase was observed for changes in maximum oxygen consumption ($\bar{X}$ ±SD=1.86±2.17 mL/kg^{-1}min^{-1}; 95% CI=0.31–3.41). No statistically significant or clinically important changes were found for any of the other secondary outcomes.

Discussion

One of the primary roles of a meta-analysis is to attempt to arrive at some overall conclusion(s) regarding a particular body of research. The overall results of this study suggest that aerobic exercise has a small but positive effect on BMD at the lumbar spine and femur in both premenopausal and postmenopausal women, and that this effect appears to be the result of increasing and/or preserving BMD. The fact that a similar effect was not found at the radius is not surprising, given that it appeared that all of the exercise interventions that the studies employed focused on

Table III. Overall Results for BMD

VARIABLE	ES(#)	$\bar{X}$±SD	95% CI	Q(P)
Lumbar spine	31	0.33±0.49	0.16 to 0.50*	33.65 (0.29)
Femur	42	0.25±0.35	0.14 to 0.35*	32.93 (0.81)
Radius	10	0.10±0.45	−0.20 to 0.41	09.99 (0.44)

BMD=bone mineral density; CI=confidence interval.
* Significantly different from zero.

loading the lower extremities. Thus, specific loading at all sites, including the radius, may be necessary in order to help increase and/or preserve BMD at that particular site. The overall results observed in this study are similar to those of our previous and less complete work, in which comparable changes in BMD were reported.[5–7]

While the results of this study are positive with respect to changes in BMD at the lumbar spine and femur, the clinical importance of such small changes (approximately 2%) is not known, especially as they relate to fracture risk. Indeed, it may be that postmenopausal women might need other types of nonpharmacologic and pharmacologic interventions in addition to, or in lieu of, aerobic exercise in order to realize a significant impact on increasing and/or preserving BMD and subsequently reducing fracture risk. For example, a recent meta-analysis found that 10 mg per day of alendronate over a period of 3 years in postmenopausal, osteoporotic women reduced the estimated cumulative incidence of nonvertebral fractures from 12.6% in the placebo group to 9.0% in the alendronate group.[41] This coincided with an increase in BMD of approximately 8.8% at the spine, 7.8% at the trochanter, and 5.9% at the femoral neck.[41] Since the changes in BMD observed in this meta-analysis were much smaller, it is difficult to generalize as to how these changes impact subsequent fracture risk. It would appear plausible to suggest that future studies examining the effects of exercise on changes in BMD attempt to address the clinical importance of these changes on subsequent fracture risk.

The fact that there were greater changes in BMD at the femur in those studies that included calcium supplementation suggests that its combination with exercise may be necessary in order to increase and/or preserve BMD in women. This supports previous work in which calcium supplementation was found to be necessary in order to maximize the benefits of exercise on BMD.[42]

We were surprised to find that both higher and lower impact activity yielded similar benefits at both the femur and lumbar spine, especially since it is generally believed that higher impact activity will have a more positive effect on BMD. However, our results support other reports of similar BMD results for both higher and lower impact activities.[22] This notwithstanding, our results need to be interpreted with caution, since the issue of mechanical loading and skeletal integrity is still a controversial area in need of additional research.[43] Furthermore, since few authors reported the specific ground-reaction forces associated with the intervention employed, we were limited to developing a somewhat arbitrary classification system.

Despite the fact that meta-analysis is a quantitative approach for reviewing a body of literature, subjective decisions still have to be made. For example, in this investigation, we chose to include unpublished studies (dissertations) in our analysis. While the inclusion of unpublished studies in scientific overviews is controversial, we believe that if appropriate resources are available, unpublished studies should not be systematically excluded. Rather, they should be included and examined for potential differences when compared to published work. This is especially true given the fact that there is a bias toward publishing studies that yield statistically significant and positive results. For example, Sterling et al.[44] found that approximately 96% of selected psychology journals and 85% of selected medical journals published studies that yielded a statistically significant result. The inclusion of unpublished work in scientific overviews is a feeling that is shared by the vast majority of meta-analysts and methodologists; approximately 78% believe that unpublished material should definitely or probably be included in scientific overviews.[45] Alternatively, it may be argued that the inclusion of unpublished work is inappropriate because it has not gone through the peer review process and/or that such studies were never submitted for publication consideration because of the feeling that they may have been flawed because of some type of methodologic problem. However, the fact that we found no statistically significant difference in study quality between published and unpublished work and found no difference in ES results when our data were partitioned according to type of publication led us to include this information in our analysis.

Another subjective decision we made was the inclusion of nonrandomized, controlled trials. We believe that it is important to include nonrandomized trials, at least in the exploratory phase, in order to see if they differ from randomized trials. Since our subgroup analyses revealed no statistically significant differences in ES between randomized and nonrandomized trials at any of the sites assessed, we chose to include these in our final analysis.

While it appears that aerobic, site-specific exercise has a small but positive effect on BMD in adult women, these results need to be interpreted with regard to the following caveats. First, the fact that our

funnel plot analysis was suggestive of publication bias for both lumbar spine and femur results may warrant caution in the interpretation of our findings. We chose to use this quasi-statistical approach because the statistical approaches that have been developed to date are not grounded in formal statistical theory and make assumptions that are doubtful or indefensible.[46] However, it is also important to realize that the sensitivity of funnel plots for detecting publication bias has not been assessed systematically.[46] Second, the very nature of meta-analysis dictates that the meta-analysis itself inherits the limitations of the studies included in the analysis. For example, we were unable to perform subgroup analyses of ES changes in BMD at the lumbar spine according to whether drugs were taken that could enhance BMD, cigarette smoking, diet, previous physical activity habits, and the specific site at which BMD was assessed. In addition, insufficient information was available to examine ES changes in BMD at both the lumbar spine and femur according to alcohol consumption, previous fractures, and training modality. Furthermore, we were limited to conducting simple vs. multiple regression analysis because of missing data. The ability to include this missing information may have yielded some interesting results. However, while missing data is a common problem in meta-analytic research, it should not preclude one from conducting a quantitative review. In fact, one of the reasons for conducting a meta-analysis is to identify areas of weakness and provide directions for future research. With the former in mind, we believe that future studies should include, and editors publish, complete information regarding whether any drugs were taken that could enhance BMD, cigarette smoking, diet, previous physical activity habits, alcohol consumption, and previous fractures. In addition, future studies should probably assess and report the different ground-reaction forces associated with the physical activity interventions they employ. We believe that this is critical to the establishment of more precise guidelines aimed at enhancing BMD.

In conclusion, the overall results of this study suggest that aerobic exercise has a small but positive effect on BMD at the lumbar spine and femur in women. ■

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Exercise and Lumbar Spine Bone Mineral Density in Postmenopausal Women: A Meta-Analysis of Individual Patient Data

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Background. Low bone mineral density (BMD) at the lumbar spine is a major public health problem among postmenopausal women. We conducted a meta-analysis of individual patient data (IPD) to examine the effects of exercise on lumbar spine BMD in postmenopausal women.

Methods. IPD were requested from a previously developed database of summary means from randomized and nonrandomized trials dealing with the effects of exercise on BMD. Two-way analysis of variance tests with pairwise comparisons ($p \leq .05$) and 95% confidence intervals (CIs) were used to determine the statistical significance for changes in lumbar spine BMD.

Results. Across 13 trials that included 699 subjects (355 exercise, 344 control), a statistically significant interaction was found between test and group ($F = 15.232$, $p = .000$). Pairwise comparisons (Bonferroni t tests) revealed a statistically significant increase in final minus initial BMD for the exercise group ($\bar{X} \pm SD = 0.005 \pm 0.043$ g/cm^2, $t = 2.46$, $p = .014$, 95% CI = 0.001–0.009) and a statistically significant decrease in final minus initial BMD for the control group ($\bar{X} \pm SD = -0.007 \pm 0.045$ g/cm^2, $t = -3.051$, $p = .002$, 95% CI = −0.012–−0.002). Changes were equivalent to an approximate 2% benefit in lumbar spine BMD (exercise, +1%, control, −1%).

Conclusions. The results of this IPD meta-analysis suggest that exercise helps to improve and maintain lumbar spine BMD in postmenopausal women.

IT has been estimated that approximately 26.2 million postmenopausal women have either osteoporosis or osteopenia (1). As a result of having osteoporosis or osteopenia, a person is at an increased risk for fracture, particularly at the vertebrae, hip, and distal forearm (2). Of these three sites, fractures of the vertebrae, which represent approximately 56% of all fractures, are the most common, with an estimated 700,000 per year (2). The health-care costs associated with vertebral fractures were estimated to be approximately $746 million in 1995 and are expected to increase substantially in the future (3).

One of the potential interventions for increasing and/or maintaining vertebral bone mineral density (BMD) in postmenopausal women is exercise, a low-cost, nonpharmacologic intervention that is available to most individuals. We have recently conducted meta-analytic work in which we reported improvements in lumbar spine BMD because of exercise in postmenopausal women (4,5). This work was based on the most commonly used approach for conducting meta-analytic work, that is, the abstraction of summary means from studies meeting specified inclusion criteria. However, the use of individual patient data (IPD) versus summary means from eligible studies represents the most comprehensive approach for conducting meta-analytic work, including the potential for increased statistical power as well as a more thorough examination of potential covariates (6–8). Given the health-care consequences of low BMD at the lumbar spine, the possible benefit of exercise for improving and/or maintaining lumbar spine BMD, and the potential for a meta-analysis of IPD to provide more thorough information regarding the effect of exercise on lumbar spine BMD, we sought to examine the effects of exercise on lumbar spine BMD in postmenopausal women by conducting a meta-analysis using IPD.

Methods

Data Sources

From a previously developed meta-analytic database that included the summary means from 76 studies dealing with the effects of exercise on BMD, we sought to obtain IPD. Briefly, IPD were requested by sending a cover letter and data request sheet to authors via postal mail. For those who did not respond to our initial request, a follow-up letter was sent via postal mail approximately 5 weeks later.

Study Selection

From the database of 76 studies, we included studies that met the following criteria: (i) randomized and nonrandomized trials that included a comparative control (nonexercise) group, (ii) exercise lasting at least 16 weeks, (iii) postmenopausal women only, (iv) journal articles, dissertations, and masters theses published in the English-language literature, (v) studies published between January 1966 and December

1998, (vi) BMD (relative value of bone mineral per measured bone area) assessed at the lumbar spine, and (vii) ability to obtain IPD from authors. Despite the fact that methods to assess BMD (dual-photon absorptiometry [DPA], dual-energy x-ray absorptiometry [DEXA]) have only been widely available since the 1980s, we searched back to 1966 to ensure that there was no comparative technology that we might have missed. We did not include studies from non-English-language journals because of the potential for error in the translation and interpretation of findings. If more than one study included the same subjects, for example, a dissertation and refereed journal article, we retrieved and referenced both studies to extract the maximum amount of information but only included this as one data set.

Data Abstraction

All data were abstracted on a coding sheet that could hold up to 91 pieces of information from each study. All data were coded and verified for accuracy and consistency by George A. Kelley. Blinding of the coder to the identity and institutional affiliation of the authors as well as study results was not performed because it has been shown that these procedures have neither a statistically significant nor a clinically important effect on the results (9). The major categories coded included study, subject, BMD assessment, and training program characteristics as well as primary and secondary outcomes.

Statistical Analysis

Initial subject characteristics.—Potential differences between initial subject characteristics for exercise and control groups were examined using independent t tests and 95% confidence intervals (CIs) for continuous variables and 2×2 chi-square tests for categorical variables.

Primary outcomes.—Initial and final values for lumbar spine BMD between exercise and control groups were examined by using a two-way analysis of variance (ANOVA) test with repeated measures on one factor (test). Because this was an unbalanced design, a General Linear Model was used. Pairwise comparison tests (Bonferroni t tests) were used to identify the specific location of the observed interaction between test (final vs initial) and group (exercise vs control). To examine for outliers, ANOVAs were performed with each study deleted from the model once. Because of missing data, we were unable to include potential covariates in the ANOVA model. Consequently, we used Pearson-Product moment correlations to examine for potential associations between changes in BMD and age, height, body weight, years postmenopausal, cigarette smoking, alcohol consumption, calcium and vitamin D intake, compliance (percentage of exercise sessions attended), length of training (weeks), type of BMD assessment (DEXA, DPA), and study design (randomized vs nonrandomized controlled trial). We were unable to partition the data according to the different types of exercise because of the various interventions employed.

Because of the inability to retrieve IPD from all eligible studies, we also examined whether our results differed between studies according to the availability of IPD. To include all eligible studies in the analysis, we used the standardized difference effect size (ES) calculated from the summary data reported in the studies and corrected for small sample bias (10). In general, an ES of 0.20 is considered a small effect, 0.50 a moderate effect, and 0.80 a large effect (11). An ES of 0.80, for example, means that the exercise group differed from the control group by eight-tenths of a standard deviation in favor of the exercise group. We then compared ES differences between those studies in which IPD were provided versus those in which they were not using an ANOVA-like random effects model developed for meta-analytic research (10). This was accomplished by examining the between (Q_b) and within (Q_w) group differences for the ESs and their variances from each group.

Secondary outcomes.—Secondary outcomes (body weight, calcium intake, and vitamin D intake) were analyzed using the same ANOVA procedures that were used to evaluate changes in lumbar spine BMD. We used independent t tests to analyze initial differences between exercise and control groups for these variables because more data were available for initial values versus final values and we wanted to capture as much data as possible in our analyses.

Descriptive Statistics and Alpha Level

Means and standard deviations ($\bar{X} \pm SD$) were used to describe continuous variables, whereas frequencies and percentages were used for categorical variables. The alpha level for statistical significance was set at $p \leq .05$. Ninety-five percent CIs that did not cross 0.00 were also considered statistically significant.

Results

Study Characteristics

Of the 32 studies that met our criteria for inclusion, we were able to retrieve IPD from 13 (41%) (12–26). Note that the number of references exceeds the number of studies because two were published in dissertation (17,24) and two in journal format (18,25). A description of the studies is shown in Table 1. The 13 studies represented a total of 30 groups (17 exercise, 13 control) and 699 subjects (355 exercise, 344 control). Seven of the trials were randomized controlled trials, and the remaining six were nonrandomized controlled trials. The length of the studies ranged from 24 to 104 weeks ($\bar{X} \pm SD = 56 \pm 8$ weeks). Thirteen of the exercise groups included some type of weight-bearing exercise, two appeared to perform nonweight-bearing exercise, and the remaining two participated in weight training. Compliance, defined as the percentage of exercise sessions attended, averaged 75 ± 17%. Seven of the studies assessed lumbar spine BMD using DEXA, whereas the remaining six used DPA.

Initial Subject Characteristics

Initial subject characteristics for continuous and categorical variables can be found in Tables 2 and 3, respectively. For continuous variables, the number of years that the subjects were postmenopausal was significantly greater in the control versus exercise groups, whereas calcium intake was

Table 1. Characteristics of Bone Mineral Density Studies (gm/cm^2) in Which IPD Were Provided for Postmenopausal Women at the Lumbar Spine

Study	Design/Subjects	Exercise Intervention(s)	BMD Assessment
Bloomfield and colleagues (12)	CT that included 18 postmenopausal women assigned to either an exercise (n = 7; age = 62.1 ± 2.1 years) or control (n = 11; age = 60.0 ± 9.4 years) group.	32 weeks of training performed 3× per week for 50 minutes per session (15-minute warm-up, 30 minutes of stationary cycling, 5-minute cool-down) at 60–80% of maximal heart rate.	DPA (Lunar DP3, Lunar Radiation, Madison, WI) at L1–L4.
Bravo and colleagues (13)	RCT that included 106 women assigned to either an exercise (n = 44; age = 59.8 ± 5.9 years) or control (n = 62; age = 60 ± 6.3 years) group.	52 weeks of training performed 3× per week for 60–65 minutes per session. Exercise sessions consisted of a 10-minute warm-up, 25 minutes of rapid walking replaced with aerobic dance 1× per week, and 15 minutes of bench stepping at 60–70% of MHRR. This was followed by 10–15 minutes of resistance exercise.	DEXA (Lunar DPX, Lunar Radiation) at L2–L4.
Brooke-Wavell and colleagues (14)	RCT of 76 postmenopausal women assigned to either an exercise (n = 37; age = 65.0 ± 2.8 years) or control (n = 39; age = 64.2 ± 3.1 years) group.	52 weeks of training that consisted of self-monitored walking 3.5 times per week for 14.8 minutes per day for the first 12 weeks, followed by 20.4 minutes per day of walking, 4.8 days per week, for the remainder of the study.	DEXA (Lunar DPX, Lunar Radiation) at L2–L4.
Caplan and colleagues (15)	CT of 30 postmenopausal women assigned to either an exercise (n = 19; age = 66.4 ± 5.0 years) or control (n = 11; age = 65.4 ± 4.9 years) group.	104 weeks of aerobic weight-bearing exercise performed 2× week for 60 minutes (warm-up, 20–25 minutes of low-impact aerobic exercise, 10 minutes of ball games for improved hand-eye coordination followed by work on floor mats for strength and flexibility, 10 minutes of relaxation). Subjects were also asked to exercise on their own 1× per week so that the pulse would be elevated for at least 20–30 minutes.	DPA (Lunar DPA, Lunar Radiation).
Ebrahim and colleagues (16)	RCT of 92 postmenopausal women assigned to either an exercise (n = 47; age = 66.4 ± 7.9 years) or control (n = 45; age = 68.1 ± 7.8 years) group.	104 weeks of walking 3× per week for 40 minutes per session.	DEXA (Lunar DPX, Lunar Radiation).
Grove (17), Grove and Londeree (18)	RCT that included 15 postmenopausal women assigned to either a low-impact exercise group (n = 5; age = 56.6 ± 43.3 years), high-impact exercise group (n = 5; age = 54.0 ± 1.9 years), or control group (n = 5; age = 56.0 ± 4.5 years).	52 weeks of training performed 3× week for approximately 60 minutes per session (15–20 minute warm-up, 20 minutes of either low- or high-impact exercise, 15-minute cool-down). Low-impact activities were considered those that produced forces less than 1.5× body weight, high impact ≥2.0× body weight.	DPA (Lunar DP3, Lunar Radiation) at L2–L4.
Iwamoto and colleagues (19)	CT that included 35 postmenopausal women assigned to either an exercise (n = 15; age = 64.8 ± 6.1 years) or control (n = 20; age = 64.8 ± 5.7 years) group.	52 weeks of outdoor walking (7 days per week) and gymnastic training (at least 5 days per week).	DEXA (Norland XR26, Norland Medical Systems, White Plains, NY) at L2–L4.
Little (20)	CT that included 21 postmenopausal women assigned to a resistance training (n = 6; age = 59.5 ± 2.3 years), walking (n = 6; age = 52.3 ± 4.5 years), swimming (n = 5; age = 51.8 ± 5.8 years), or control (n = 4; age = 60.8 ± 1.4 years) group.	Resistance exercise consisted of 32 weeks of training with 9 exercises performed 3 times per week for 1 set of 8–12 repetitions at 60%–80% of 1RM; Walking consisted of 32 weeks of training, 3× per week for 30–50 minutes per session (5–10-minute warm-up; walking for 20–30 minutes; 5–10-minute cool-down) at 70%–90% of maximal heart rate; Swimming consisted of 32 weeks of training, 3× per week for 30–50 minutes per session (5–10-minute warm-up; walking for 20–30 minutes; 5–10-minute cool-down) at 70%–90% of maximal heart rate.	DPA (Lunar, Lunar Radiation) at L2–L4.
Lord and colleagues (21)	RCT that included 138 subjects assigned to either an exercise (n = 67; age = 70.8 ± 5.0 years) or control (n = 69; age = 71.0 ± 4.9 years) group.	42 weeks of exercise performed 2× per week for approximately 60 minutes per session (5-minute warm-up, 35–40 minutes of aerobic exercises [activities for balance, hand-eye and foot-eye coordination], strengthening exercises, 15 minutes of stretching, and 5–10 minute cool-down).	DEXA (Lunar DPX, Lunar Radiation) at L2–L4.
Martin and Notelovitz (22)	RCT that included 55 postmenopausal women assigned to a 30-minute exercise group (n = 20; age = 60.3 ± 7.8 years), 45-minute exercise group (n = 16; age = 57.8 ± 7.1 years), or control (n = 19; age = 56.7 ± 6.9 years) group.	52 weeks of treadmill exercise performed 3× week for either 30 or 45 minutes per session at 70–85% of maximal heart rate. Each session included a 3–5-minute warm-up and cool-down at 60% of maximal heart rate.	DPA (Lunar DP3, Lunar Radiation) at L2–L4.

Continued on next page

Table 1. Characteristics of Bone Mineral Density Studies (gm/cm^2) in Which IPD Were Provided for Postmenopausal Women at the Lumbar Spine (*Continued*)

Study	Design/Subjects	Exercise Intervention(s)	BMD Assessment
Prince and colleagues (23)	RCT that included assignment of 63 postmenopausal women to a calcium and exercise (n = 35; age = 62.4 ± 4.8 years), or calcium only (n = 28; age = 63.2 ± 4.8 years) group.	104 weeks of weight-bearing exercise performed 2× week for approximately 60 minutes per session. Subjects were also asked to walk another 2 hours per week at 60% of peak heart rate for their age.	DEXA (QDR-1000, Hologic, Waltham, MA) at L1–L4.
Pruitt (24), Pruitt and colleagues (25)	CT that included 24 postmenopausal women assigned to either an exercise (n = 15; age = 53.6 ± 4.1 years) or control (n = 9; age = 55.6 ± 2.9 years) group.	36 weeks of strength training consisting of 13 exercises performed 3× week at 50%–60% of 1RM for 1 set of 10–12 repetitions for the upper body and 10–15 repetitions for the lower body.	DPA (Lunar DP3, Lunar Radiation) at L2–L4.
Ryan and colleagues (26)	CT that included 28 postmenopausal women assigned to either a weight loss (n = 15; age = 63.4 ± 5.7 years) or exercise + weight loss (n = 13; age = 61.3 ± 4.8 years) group.	24 weeks of aerobic exercise (treadmill jogging) performed 3× week for up to 35 minutes per session at 50 to >70% of $\dot{V}O_{2max}$. Each session included a 10-minute warm-up and cool-down period.	DEXA at L2–L4.

Notes: IPD = individual patient data; BMD = bone mineral density; CT = controlled trial; RCT = randomized controlled trial; DPA = dual-photon absorptiometry; DEXA = dual-energy x-ray absorptiometry; MHRR = maximal heart rate reserve; RM = repetition maximum. Study by Prince also included placebo and milk powder group but for comparison purposes, these groups were not included in our analysis. Only subjects who completed the study and for which BMD data were available are reported in the designs/subjects section; number of subjects reported as $\bar{X} \pm SD$. Bone density assessment limited to bone mineral density measures in g/cm^2.

greater in the exercise versus control groups. No statistically significant differences between exercise and control groups were observed for any other continuous or categorical variables.

Primary Outcomes

As can be seen in Table 4, there was an increase in lumbar spine BMD in the exercise groups and a decrease in the control groups. The mean difference between the two groups was 0.013 ± 0.079 g/cm^2, 95% CI = 0.007–0.019. These changes were equivalent to an approximate 2% benefit in lumbar spine BMD (exercise, +1%, control, −1%). The ANOVA results in Table 5 show a statistically significant main effect difference between group and an interaction between group and test. Pairwise comparison tests for the Group × Test interaction revealed a statistically significant increase in final versus initial BMD for the exercise groups (t = 2.464, p = .014), a statistically significant decrease in final versus initial BMD for control groups (t = −3.051, p = .002), and greater initial as well as final values for exercise groups compared to control groups (initial, t = 2.544, p = .011; final, t = 3.320, p = .001). Results were similar when each study was deleted from the model once. For the exercise groups, larger increases in lumbar spine BMD were associated with assessment of BMD using DEXA versus DPA (r = −0.126, p = .018, 95% CI = −0.227–−0.022). For control subjects, larger decreases in lumbar spine BMD were associated with younger age (r = 0.170, p = .002, 95% CI = 0.064–0.272), taller stature (r = −0.109, p = .048, 95% CI = −0.215–−0.005), absence of hormone replacement therapy (r = 0.152, p = .005, 95% CI = 0.047–0.254), assessment of BMD using DPA versus DEXA (r = −0.287, p = .000, 95% CI = −0.381–−0.187) and nonrandomized versus randomized controlled trials (r = 0.172, p = .001, 95% CI = 0.067–0.273). No other statistically significant or clinically relevant relationships were observed for the exercise or control groups. Finally, no statistically significant differences in lumbar spine BMD were found when we compared the 13 studies that included IPD (ES = 0.366 ± 0.423, 95% CI = 0.131–0.600) with the 19 studies that did not include IPD (ES = 0.219 ± 0.430, 95% CI = 0.059–0.379; Q_b = 1.184, p = .277).

Secondary Outcomes

No statistically significant main effects or interactions were found for body weight, calcium intake, or vitamin D intake.

Discussion

The primary purpose of meta-analysis is to reach some general conclusions about a body of research. The overall results of this study suggest that exercise helps to in-

Table 2. Initial Characteristics of Subjects for Continuous Variables

Variable	n	Exercise $\bar{X} \pm SD$	n	Control $\bar{X} \pm SD$	Significance t (p)	CI (95%)
Age (y)	340	63.9 ± 7.4	335	64.5 ± 7.4	−0.92 (.357)	−1.64 to 0.59
Height (cm)	329	158.9 ± 6.9	327	158.2 ± 7.0	1.18 (.239)	−0.43 to 1.71
Body Weight (kg)	340	65.1 ± 12.3	330	64.1 ± 13.0	1.04 (0.299)	−0.91 to 2.94
Postmenopause (y)	156	13.0 ± 9.9	147	17.3 ± 11.8	−3.46 (.001)*	−6.78 to −1.86*
Calcium (mg)	193	926.9 ± 394.0	195	834.7 ± 350.6	2.44 (.015)*	17.79 to 166.64*
Vitamin D (IUs)	55	195.9 ± 215.4	62	161.5 ± 132.4	1.05 (.294)	−30.27 to 99.13

Note: CI = confidence interval; IUs = international units.
*Statistically significant.

Table 3. Initial Characteristics of Subjects for Categorical Variables

Variable	Exercise *n* (%)	Control *n* (%)	χ_2 (*p*)
Cigarette Smoking	25 (9.9)	33 (12.7)	1.04 (.307)
Alcohol Consumption	130 (52.2)	121 (47.5)	1.14 (.285)
Estrogen/Progesterone Use	24 (6.9)	18 (5.4)	0.65 (.419)
Previous Fractures (any site)	61 (37.4)	62 (41.6)	0.57 (.450)
Race (white)	259 (94.1)	238 (91.2)	1.78 (.182)

Note: Results limited to studies that reported data for each variable.

Table 5. ANOVA Summary Table for Lumbar Spine BMD (General Linear Model)

Source of Variation	*df*	SS	*MS*	*F*	*p*	Partial η^2
Group	1	0.834	0.834	8.685	.003*	0.012
Error (Group)	697	66.962	0.096	—	—	—
Test	1	0.000	0.000	0.199	.656	0.000
Test × Group	1	0.001	0.001	15.232	.000*	0.021
Error (Test)	697	0.670	0.001	—	—	—

Note: SS = sum of squares; *MS* = mean square; Group = exercise vs control; Test = initial vs final.

*Significantly different, $p \leq .05$.

crease and maintain lumbar spine BMD in postmenopausal women. This supports our previous meta-analytic work of summary means and lumbar spine BMD (4,5), but is in contrast to our more recent meta-analytic work using IPD in which we found no statistically significant difference in femoral neck BMD (27). Although these are important findings, the clinical importance of an approximate 2% benefit, especially as it relates to fracture risk, cannot be elucidated at this time. However, although beyond the scope of this study, the increased strength, balance, and ambulatory skills that may be realized from a regular program of exercise may also help reduce the risk of falling and suffering subsequent fractures (28). Although we were unable to identify specific exercise programs for optimizing lumbar spine BMD, it would appear plausible to suggest that one adhere to the recent National Institutes of Health Consensus Statement that recommends participation in regular exercise, especially resistance and high-impact activities (28).

Our finding that larger decreases in BMD in the control groups were associated with younger age is not surprising given the fact that bone loss is most rapid during the early postmenopausal years (29). In addition, the observed association between the absence of hormone replacement therapy and greater decreases in lumbar spine BMD was also not surprising because hormone replacement therapy is an established therapeutic intervention for preserving BMD among postmenopausal women (28). However, we can offer no biological explanation regarding the observed association between greater decreases in lumbar spine BMD and taller stature. This is especially because it is generally believed that shorter women are considered more osteoporotic than taller women. Given this currently held notion, caution is warranted in the interpretation of this finding. Indeed, it may be that our observed association was nothing more than the play of chance given the large number of statistical tests that were conducted in our study.

Meta-analysis, like any other type of review, is limited by the availability of data and the limitations of the included studies. Thus, in addition to making the best of the existing data and trying to reach some overall conclusions regarding a body of research, it is also the meta-analyst's responsibility to identify areas of weakness to provide directions for future research.

For example, because we were unable to categorize the different types of exercise interventions, we would suggest that future researchers provide a better description of their exercise programs, especially as it relates to the forces employed during the exercise intervention. Consequently, exercise programs that provide optimal benefits to lumbar spine BMD can be recommended.

We were surprised that data on calcium intake were available for only 56% of the subjects included in this analysis. Because calcium intake is important for maintaining and/or increasing BMD in humans, it would seem reasonable to suggest that data on calcium intake be assessed and reported. In addition, because vitamin D intake is also important for the absorption of calcium and data on vitamin D intake were available for only 17% of the subjects included in this analysis, the assessment and reporting of this information also appears warranted.

Although white, non-Hispanic women are disproportionately affected with osteoporosis and low bone mass, the effect on other races is also significant. For example, the National Osteoporosis Foundation has reported that approximately 10% of black women older than 50 years have osteoporosis, and 29% have low bone mass. Additionally, 16% of American-Indian and Hispanic women aged 50 and older have osteoporosis, and 36% have low bone mass (30). Because approximately 93% of the subjects in this study were white and the responses to exercise in relation to BMD may vary by race, it is recommended that future studies include women from other ethnic groups.

Because data on the number of years that the subjects were postmenopausal were available for only 43% of the subjects included in this analysis, future research needs to include this type of information because it may be a potential confounder in relation to exercise-induced changes in lumbar spine BMD in postmenopausal women.

The fact that the vast majority of studies included in our meta-analysis were published in refereed journal articles may have led to an overestimate of the benefits of exercise on BMD at the lumbar spine because there is a tendency for authors to submit, and editors to publish, studies that yield statistically significant and positive results, i.e., publication bias (10).

Table 4. Lumbar Spine BMD Results (g/cm^2)

Group	*n*	Initial ($\bar{X} \pm SD$)	Final ($\bar{X} \pm SD$)	Difference ($\bar{X} \pm SD$)	CI (95%)
Exercise	355	0.991 ± 0.221	0.996 ± 0.224	0.005 ± 0.043	0.001 ± 0.009*
Control	344	0.948 ± 0.218	0.941 ± 0.218	−0.007 ± 0.045	−0.012 ± −0.002*

Note: CI = confidence interval.

*Statistically significant.

For both exercise and control subjects, greater decreases in lumbar spine BMD were associated with assessment of BMD using DPA versus DEXA. Because DEXA is generally considered to be a more valid assessment of BMD and is currently the most common method used to assess BMD at the lumbar spine, the results from studies using DEXA may be more valid. The finding that greater decreases in lumbar spine BMD were associated with nonrandomized versus randomized trials suggests that randomized trials may yield more valid results.

Although the above-described associations are interesting, they should be viewed with caution for the following reasons: (i) they may have been nothing more than the play of chance given the large number of statistical tests that were conducted, (ii) we were unable to examine for potential interrelationships between variables because of missing data, and (iii) the associations accounted for only a small proportion of the total variance.

In conclusion, the results of this IPD meta-analysis suggest that exercise improves and maintains lumbar spine BMD in postmenopausal women.

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Efficacy of Resistance Exercise on Lumbar Spine and Femoral Neck Bone Mineral Density in Premenopausal Women: A Meta-Analysis of Individual Patient Data

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ABSTRACT

Background: **Osteoporosis and osteopenia are major public health problems. The purpose of this study was to conduct an individual patient data (IPD) meta-analysis to examine the efficacy of resistance exercise on lumbar spine and femoral neck bone mineral density (BMD) in premenopausal women.**

Methods: **Studies were retrieved via (1) computerized literature searches, (2) review of reference lists from previous studies, (3) hand searching selected journals, and (4) expert review of the reference list. Two × two analysis of covariance (ANCOVA) tests with repeated measures on one factor (time) and study as a covariate were used to analyze changes in BMD.**

Results: **One hundred forty-three subjects (74 exercise, 69 control) were included in the analysis. Changes in lumbar spine BMD averaged 0.006 ± 0.035 g/cm^2 (0.64 ± 2.99%) in the exercise group and 0.008 ± 0.091 g/cm^2 (0.74 ± 7.58%) in the control group, and changes in femoral neck BMD averaged 0.005 ± 0.031 g/cm^2 (0.46 ± 3.10%) in the exercise group and 0.003 ± 0.031 g/cm^2 (0.31 ± 2.97%) in the control group. No statistically significant differences in lumbar spine or femoral neck BMD were found within or between the exercise and control groups ($p > 0.05$).**

Conclusions: **Based on existing evidence, our results do not support the efficacy of resistance exercise for increasing or maintaining lumbar spine and femoral neck BMD in premenopausal women.**

INTRODUCTION

OSTEOPOROSIS, defined as a bone mineral density (BMD) value >2.5 standard deviations (SD) below the mean, and osteopenia, defined as a BMD value between 1 and 2.5 SD below the mean,[1] are major public health problems among women aged ≥50 years in the United States and are expected to increase throughout the coming years. It is estimated that approximately 30 million women had osteoporosis or osteopenia in 2002, with this number expected to increase to approximately 41 million in 2020.[2] As it is well established that osteoporosis and osteopenia increase one's risk for fracture, particularly at the lumbar spine and femoral neck, appropriate intervention strategies are needed to maximize BMD. Especially at risk are women diagnosed with osteoporosis, particularly those in whom one or more fragility fractures are present.[1] The

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National Institutes of Health's Consensus Conference on the prevention, diagnosis, and therapy of osteoporosis recommended that reducing the prevalence of osteoporosis and osteopenia in older women may be realized by maximizing BMD during the premenopausal years.[3] As a result of maximizing BMD during this time period, a greater absolute amount of BMD may be maintained during the postmenopausal years despite the inevitable loss of some BMD during this period.

One strategy recommended for maximizing BMD during the premenopausal years is resistance exercise, a low-cost, nonpharmacological intervention that is available to most people.[2–5] Unfortunately, results from intervention studies dealing with the effects of resistance exercise on lumbar spine and femoral neck BMD in premenopausal women have been less than overwhelming. For example, only 46% of the outcomes from studies dealing with the effects of resistance exercise on lumbar spine BMD in premenopausal women have been reported as statistically significant and positive, and only 9% have been reported as statistically significant and positive at the femoral neck.[6–18] One of the possible reasons for these disappointing results may have been the inability to enroll an adequate number of subjects in most studies, thereby reducing the power to detect a statistically significant effect of resistance exercise on BMD. For example, in the previously cited studies, the total number of subjects ranged from 17 (10 exercise, 7 control) to 91 (46 exercise, 45 control). Meta-analysis is an approach in which the results of studies sharing the same outcome of interest are synthesized for the purpose of attempting to reach some general conclusions about a body of research.[19,20] One of the reasons for conducting a meta-analysis is when studies addressing the same primary outcome of interest take on one or more different characteristics.[21] These characteristics may include study design (e.g., randomized vs. nonrandomized trials), different follow-up periods, and different types of resistance training programs (e.g., high vs. moderate intensity training, upper vs. lower limb exercises). Meta-analysis is usually not appropriate when the characteristics between studies are identical because similar results should be obtained between studies containing identical characteristics.[21]

Whereas the most common type of meta-analysis is the combining of summary means from groups of subjects in each study and calculation of an overall estimate of effect, a meta-analysis of individual patient data (IPD) uses the data from each individual subject as the end point. The primary advantage of this approach is calculation of estimates of effect on a patient vs. study-level basis. Therefore, given (1) the importance of maintaining optimal BMD during the premenopausal years, particularly at the lumbar spine and femoral neck, (2) the inconsistencies in the results of studies dealing with the effects of resistance exercise on BMD at the lumbar spine and femoral neck in premenopausal women, and (3) the potential for an IPD meta-analysis to more accurately identify the effects of resistance exercise on BMD at the lumbar spine and femoral neck in premenopausal women, the purpose of this study was to conduct an IPD meta-analysis to examine the efficacy of resistance exercise for increasing and maintaining lumbar spine and femoral neck BMD in premenopausal women.

MATERIALS AND METHODS

Data sources

Computerized literature searches of papers indexed between January 1966 and December 1998 were performed using MEDLINE, Current Contents, Sport Discus, and Dissertation Abstracts International databases. The following keywords were used either alone or in various combinations for computer searches: bone, bone density, bone mineral density, exercise, physical activity, women, females, physical fitness, fitness, weight training, resistance exercise, resistance training, osteoporosis, osteopenia. The titles and abstracts of studies identified in the computerized searches were examined in order to exclude any that were clearly irrelevant. The full text of the remaining papers was retrieved, and each paper was read to determine if it contained information on the topic of interest. The reference lists from both original and review papers were also reviewed in order to identify any studies that had not been previously identified and that appeared to contain information on the topic of interest. In addition, hand searching of selected journals was performed. The search and retrieval for relevant literature was conducted by both authors. Three experts on exercise and BMD (Dr. Charlotte Sanborn, Dr. David Nichols, and Dr. Christine Snow) reviewed our reference list for thoroughness and completeness.

Study selection

The inclusion criteria for this study were (1) premenopausal women ages ≥18 years but not competitive athletes, (2) baseline and final BMD values available at the lumbar spine or femoral neck or both, (3) studies published in English language journals or as dissertations or master's theses between January 1966 and December 1998, (4) comparative control group, (5) resistance exercise as the intervention, (6) studies in which the exercise intervention lasted a minimum of 16 weeks, and (7) ability to obtain IPD. We did not include studies published in foreign language journals because of the potential for misinterpretation in the analysis of findings. Abstracts were not included because of the paucity of information provided. Multiple publication bias (the possibility that multiple publications were generated using the same data on the same subjects) was examined by looking at each study to ensure that duplicate data were not included as separate entries in the database.

For those studies that met our inclusion criteria, a cover letter and IPD request sheet were sent via postal mail to the corresponding author of each study, and a follow-up request was sent if no response was provided within approximately 5 weeks. If the corresponding author was not listed as the first author and we did not receive a response after the two mailings, we contacted the first author and requested IPD from them. Contact was also made with authors of studies in which IPD were already available in the event that additional IPD data might be provided. All authors who supplied IPD were mailed a check for $40.00 (US) to help cover incurred costs. A detailed description of this process can be found elsewhere.[22]

Data abstraction

A coding sheet was developed to record information for 91 data points. All data were coded and reviewed for accuracy and consistency by the first author. Coding was limited to one person because reliability estimates of 0.94 have been reported for meta-analyses on the same topic conducted by different and independent reviewers.[23] Blinding of the coder to the study's author and institutional affiliation was not performed because it has been shown that this does not have a statistically significant or clinically important effect on results.[24]

Statistical analysis

Baseline characteristics. Potential differences in the baseline characteristics between exercise and control subjects were examined using an independent t test for all continuous variables. Levene's test was used to examine for equality of variances between exercise and control results, with statistical adjustments made if the test was statistically significant ($p \leq 0.05$). Differences between exercise and control groups for categorical outcomes were examined using 2×2 chi-square tests with a continuity correction for any cell with an expected count of <5.

Primary outcomes. Prior to the conduct of this study, we determined that a total sample size of 128 subjects (64 per group) would be needed to detect a two-tailed standardized effect size change (d) of 0.50 (medium effect) at an alpha level of 0.05 and power of 80% for lumbar spine and femoral neck BMD, our primary outcomes for this study.[25] Changes in lumbar spine and femoral neck BMD were examined using 2×2 analysis of covariance (ANCOVA) tests with repeated measures on one factor. The between-subjects factor was group with two levels (exercise and control), and the within-subjects (repeated measures) factor was time with two levels (baseline and final BMD values). The study from which the data were derived was included as a covariate in all analyses. Statistically significant interactions between group and time were assessed using pairwise comparison tests with a Sidak adjustment for multiple comparisons. We did not include age as a covariate because we found no statistically significant relationship (Pearson's correlation coefficient) between initial BMD and age at either the lumbar spine (Pearson's $r = 0.05$, $p = 0.55$) or femoral neck ($r = -0.16$, $p = 0.18$).

Because we were unable to retrieve IPD from some studies that met our inclusion criteria, we compared summary mean effect size changes in lumbar spine and femoral neck BMD for those studies that included IPD vs. those that did not. This form of sensitivity analysis was conducted to see if the BMD results from our included studies differed from those in which we were unable to obtain IPD. In order to conduct this analysis, we first calculated a standardized effect size (d) from each study using the procedure of Hedges and Olkin.[26] Briefly, this was calculated by taking the difference in the mean change outcome

values (final minus baseline) between the exercise and control groups and dividing them by the pooled SD of the exercise and control groups.[26] All effect sizes were then adjusted for small sample bias.[26] In general, effect sizes of 0.20, 0.50, and 0.80 are considered small, medium, and large, respectively.[25] An effect size of 0.50 for example, means that the exercise group did better than the control group by 0.5 SD. After calculation of individual effect sizes, all results were pooled, and 95% confidence intervals (95% CI) using the *t* distribution were calculated.[26] Using a random-effects model, these results were subsequently dichotomized according to those studies that supplied IPD vs. those that did not and then compared using ANOVA-like methods for meta-analysis.[26] The between-groups comparison statistic for this analysis is Q_b. This statistic is similar to the between-groups *F* ratio.

Secondary outcomes. Secondary outcomes for IPD results (body weight, body mass index [BMI] in kg/m^2, lean body mass, percent body fat) were analyzed using the same procedure as for changes in BMD. Calcium intake was examined without using study as a covariate because only one study reported adequate pre-data and post-data for such.[18] We were unable to examine changes in vitamin D intake because of a lack of available data. Changes in percent strength between exercise and control groups were assessed using an independent groups *t* test.

Measures of central tendency, dispersion, and alpha. All data are reported as $\overline{X} \pm$ SD. The alpha level for all significance tests was set at $p \leq 0.05$.

RESULTS

Study characteristics

Usable IPD were available for 143 subjects (74 exercise, 69 control) from three studies.[11,14,18] We were unable to obtain IPD from nine studies.[6–10,13,15–17] Thus, our retrieval rate was 25%. One study[12] was not included because it contained some of the same subjects as one of our included studies.[18] Compliance, defined as the percentage of exercise sessions attended, averaged 86.50 ± 13.26% for the 45 subjects for whom such data were provided (approximately 59%). Seventy-one of the 143 subjects (approximately 50%) had BMD assessed using dual-energy x-ray absorptiometry (DEXA),[14,18] and the remaining 72 had BMD assessed using dual-photon absorptiometry (DPA).[11] A description of the studies is shown in Table 1.

Baseline characteristics

A description of the baseline characteristics of the subjects is shown in Tables 2 and 3. The subjects ranged in age from 18 to 47 years in the exercise group and 18 to 43 years in the control group. As can be seen, no statistically significant differences were found between the exercise and control groups for any of these variables.

Primary outcomes

Baseline and final values for BMD are shown in Table 4.

Lumbar spine BMD. Changes averaged 0.006 ± 0.035 g/cm^2 (0.64 ± 2.99%) in the exercise group and 0.008 ± 0.091 g/cm^2 (0.74 ± 7.58%) in the control group. However, no statistically significant within-subjects main effect differences were observed for time [F (1, 140) = 3.13, $p = 0.08$], or the interaction between time and group [F (1, 140) = 0.003, $p = 0.96$]. In addition, there was no statistically significant between-subjects main effect difference for group [F (1, 140) = 0.003, $p = 0.77$]. Comparison of studies that provided IPD vs. those that did not revealed no statistically significant difference between the two (IPD supplied, $d = 0.27 \pm 0.27$; IPD not supplied, $d = 0.30 \pm 0.32$, $Q_b = 0.05$, $p = 0.83$).

Femoral neck BMD. Changes averaged 0.005 ± 0.031 g/cm^2 (0.46 ± 3.10%) in the exercise group and 0.003 + 0.031 g/cm^2 (0.31 ± 2.97%) in the control group. No statistically significant within-subjects main effect differences were observed for time [F (1, 73) = 0.86, $p = 0.36$] or the interaction between time and group [F (1, 73) = 0.10, $p = 0.75$]. There was also no statistically significant between-subjects main effect difference for group [F (1, 73) = 0.10, $p = 0.75$]. Comparison of studies that provided IPD vs. those that did not revealed no statistically significant difference between the two (IPD supplied, $d = 0.27 \pm 0.28$; IPD not supplied, $d = 0.33 \pm 0.34$, $p = 0.79$, $Q_b = 0.07$, $p = 0.80$).

Table 1. Characteristics of Bone Mineral Density Studies (g/cm^2) in Which IPD Were Provided[a]

Study	*Design/subjects*	*Exercise intervention*	*BMD assessment*[b]
Gleeson et al.[11]	CT that included 67 premenopausal women assigned to either a resistance exercise (n = 32, age = 3.2 ± 6.3 years) or control (n = 35, age = 32.0 ± 5.7 years) group	52 weeks of Nautilus strength training that included 4 lower body exercises performed 3 times per week for 2 sets of 20 repetitions at 60% of 1 RM[c]	DPA (lunar) at lumbar spine
Payne[14]	CT that included 47 premenopausal women assigned to either a resistance exercise (n = 28, age = 24.6 ± 9.2 years) or control (n = 19, age = 22.8 ± 6.1 years) group	18 weeks of strength training that included 4 lower body exercises (standing calf raise, leg curl, leg press, squat) performed 3 times per week for 3–6 sets of 6–10 repetitions per exercise	DEXA (lunar) at the lumbar spine (L2–L4) and femoral neck
Vuori et al.[18]	CT that included 29 premenopausal women assigned to either a resistance exercise (n = 14, age = 21.3 ± 2.7 years) or control (n = 15, age = 22.5 ± 3.2 years) group	52 weeks of strength training that consisted of the leg press exercise performed 5 times per week for 5 sets of 10 repetitions at 80% of 1 RM	DEXA (Norland) at the lumbar spine and femoral neck

[a]Number of subjects limited to those who completed the study and had baseline and final BMD results.
[b]BMD assessment limited to BMD in g/cm^2 at the lumbar spine and femoral neck.
[c]RM, repetition maximum; DEXA, dual-energy x-ray absorptiometry; DPA, dual-photon absorptiometry.

Secondary outcomes

Baseline and final values for secondary outcomes are shown in Table 4.

Body weight. There was no statistically significant main effect difference for time [F (1, 137) = 0.15, p = 0.70] or the interaction between group and time [F (1, 137) = 1.44, p = 0.23]. There was also no statistically significant between-subjects main effects difference for group [F (1, 137) = 1.44, p = 0.23].

Body mass index. No statistically significant within-subject main effect differences were ob-

Table 2. Initial Subject Characteristics for Continuous Variables

	Exercise		*Control*			
Variable	n[a]	$\overline{X} \pm SD$	n	$\overline{X} \pm SD$	t	p
Age (years)	74	27.68 ± 8.64	69	27.38 ± 7.11	0.22	0.82
Height (cm)	46	165.29 ± 5.24	50	166.37 ± 6.61	−0.85	0.40
Body weight (kg)	73	60.28 ± 8.01	69	62.75 ± 9.41	−1.69	0.09
BMI (kg/m^2)[b]	45	21.77 ± 2.40	48	22.25 ± 2.81	−0.87	0.39
LBM (kg)	67	42.82 ± 4.61	67	43.63 ± 4.54	−1.03	0.31
Body fat (%)	51	29.25 ± 8.10	51	30.62 ± 7.68	−0.87	0.38
BMD (g/cm^2)						
Lumbar spine	74	1.197 ± 0.155	69	1.181 ± 0.142	0.66	0.51
Femoral neck	42	1.021 ± 0.130	34	1.018 ± 0.148	0.07	0.95
Menarche (age)	40	12.65 ± 1.23	32	12.72 ± 1.55	−0.21	0.83
Calcium (mg/day)	40	668.78 ± 321.96	34	778.97 ± 578.79	−0.99	0.33
Vitamin D (mg/day)	25	82.44 ± 61.83	18	69.68 ± 48.80	−0.73	0.47

[a]n, number of subjects data available for.
[b]BMI, body mass index; LBM, lean body mass; BMD, bone mineral density.

Table 3. Initial Subject Characteristics for Categorical Variables

	Exercise			Control				
Variable	n[a]	*Yes*	*No*	n	*Yes*	*No*	*Chi-square*	p
Smoking	60	3 (5.0%)	57 (95.0%)	54	4 (7.4%)	50 (92.6%)	0.02	0.89
Estrogen	60	21 (35.0%)	39 (65.0%)	54	19 (35.2%)	35 (64.8%)	0.0004	0.983

[a]*n*, number of subjects data available for.

served for time [F (1, 88) = 0.32, $p = 0.57$], nor was there a statistically significant interaction between group and time [F (1, 88) = 0.91, $p = 0.34$]. In addition, no statistically significant between-subjects main effects differences were found for group [F (1, 88) = 0.91, $p = 0.34$].

Percent body fat. No statistically significant within-subject main effect differences were observed for time [F (1, 57) = 0.22, $p = 0.64$]. However, there was a statistically significant within-subjects interaction between time and group [F (1, 57) = 10.32, $p = 0.002$]. There was also a statistically significant between-subjects main effect difference for group [F (1, 57) = 7.55, $p = 0.008$). Pairwise comparisons to test for the significant interaction between group and time revealed a statistically significant increase of 2.17 ± 4.47% ($p < 0.001$) in percent body fat for the control group.

Lean body mass. There were no statistically significant within-subjects main effects differences for time [F (1, 85) = 3.02, $p = 0.09$] or the interaction between group and time [F (1, 85) = 0.02, $p = 0.90$]. In addition, there were no statistically significant between-subjects main effect differences for group [F (1, 85) = 1.24, $p = 0.27$].

Calcium intake. A statistically significant within-subjects main effect difference was found for time [F (1, 26) = 7.84, $p = 0.01$] but not the interaction between time and group [F (1, 26) = 1.22, $p = 0.28$). There was no statistically significant between-subjects main effect difference for group [F (1, 26) = 1.51, $p = 0.23$].

Changes in strength. A statistically significant increase in strength was found in the exercise group compared with the control group [exercise, 51.57 ± 33.20%; control, 6.76 ± 13.04%; t (71.67) = 9.00, $p < 0.001$].

DISCUSSION

The primary purpose of meta-analysis, whether results are null or positive, is to summarize the available literature on a given topic in order to reach some general conclusions about a body of research. Although resistance exercise should almost always be recommended because of the numerous benefits that can be derived from it, the results of our study suggest that resistance exercise has little effect on lumbar spine and femoral neck BMD in premenopausal women de-

Table 4. Baseline and Final Values for Primary and Secondary Outcomes

	Exercise			Control		
Variable	n[a]	*Baseline*	*Final*	n	*Baseline*	*Final*
BMD (g/cm^2)[b]						
Lumbar spine	74	1.197 ± 0.155[c]	1.203 ± 0.143	69	1.181 ± 0.142	1.189 ± 0.162
Femoral neck	42	1.021 ± 0.130	1.025 ± 0.134	34	1.018 ± 0.148	1.021 ± 0.150
Body weight (kg)	73	60.28 ± 8.01	60.18 ± 8.05	67	62.87 ± 9.53	63.38 ± 10.26
BMI (kg/m^2)	45	22.77 ± 2.40	21.87 ± 2.79	46	22.30 ± 2.86	25.20 ± 20.16
Body fat (%)	33	32.59 ± 7.50	32.31 ± 7.04	27	34.80 ± 6.82	36.87 ± 8.23*
LBM (kg)	47	41.77 ± 4.01	41.62 ± 3.80	41	43.20 ± 4.60	43.12 ± 5.43
Calcium (mg/day)	13	804.62 ± 440.90	1267.77 ± 4.23	15	1081.33 ± 747.58	1282.00 ± 4.47

[a]*n*, number of subjects data available for.
[b]BMI, body mass index; LBM, lean body mass; BMD, bone mineral density.
[c]Data reported as $\overline{X}$ ± SD.
*Statistically significant increase from baseline value ($p \leq 0.05$).

spite statistically significant increases in muscular strength. The lack of statistically significant findings in our study is in agreement with the vast majority of previous studies addressing the effects of resistance training on BMD in premenopausal women.[6–18] These results differ from a summary means meta-analysis in postmenopausal women in which a small but statistically significant improvement of approximately 1% was found across all BMD sites as a result of resistance training.[27] Unfortunately, insufficient data were available to partition results according to specific BMD sites in this previous meta-analysis. In addition, there was a large amount of heterogeneity among study results.[27] Our results are also in contrast to a previous summary means meta-analysis in which an approximately 2% benefit was derived from aerobic exercise at both the lumbar spine and femur (all sites), with no statistically significant differences observed between premenopausal and postmenopausal women.[28]

Several factors may be thought to account for the lack of statistically significant findings in this meta-analysis. First, despite the fact that we included the study from which the data were derived as a covariate, it may be that the resistance exercise programs included in all the studies did not adequately load the lumbar spine and femoral neck in premenopausal women. For example, the study by Vuori et al.[18] consisted of a leg press exercise performed five times per week. Given that it is generally believed that the effects of exercise on BMD are site-specific,[29] this training program may not have been specific enough to have an effect on lumbar spine BMD. However, the results obtained in this study did not differ from the results obtained in our other two included studies. It has also been suggested that exercises designed to increase BMD at the hip should be performed while the subjects are standing on both feet.[30] Unfortunately, only one exercise (squat) from one of the studies included in our analysis[14] met the aforementioned criteria. Again however, the results obtained in this study did not differ from results obtained in the other two included studies. Furthermore, it has been suggested that the greatest improvements in BMD may occur when the resistance exercise protocols use "free" vs. machine weights.[29] However, with the exception of the squat exercise from the investigation by Payne,[14] the studies included in our analysis appeared to use machine weights for all exercises that required external apparatus. Again, though, the results of this study did not differ from the results of the other two included studies.

A second possible reason for the lack of statistically significant findings may be because optimal BMD usually is present during the premenopausal years. Consequently, little positive effects may be gained from a traditional program of resistance exercise during this time. Alternatively, it may be that resistance exercise programs of longer duration than those currently conducted would yield results demonstrating improvements and maintenance of BMD among those participating vs. not participating in a program of resistance exercise.

Despite optimal levels of BMD in most premenopausal women, improvements may still be possible if the load is high enough,[31] although the practicality of higher-intensity programs may be questioned. For example, only 15% of adult females ages $\geq$18 years reported participation in a regular program of muscular strength and endurance exercise.[32]

A third possible reason for the lack of statistically significant findings in this investigation may have to do with the fact that we were able to obtain IPD from only approximately 25% of the eligible studies. However, as we found no statistically significant differences in BMD between the summary mean results of those studies in which we were able to retrieve IPD vs. those in which we were not, we believe that our results are an adequate representation of the data currently published in this area.

In conclusion, our results suggest that the currently available literature does not support the efficacy of resistance exercise for increasing or maintaining lumbar spine and femoral neck BMD in premenopausal women.

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Exercise and bone mineral density at the femoral neck in postmenopausal women: A meta-analysis of controlled clinical trials with individual patient data

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KEY WORDS
Exercise
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Objective: We conducted a meta-analysis using individual patient data to examine the efficacy of exercise for improving bone mineral density at the femoral neck in postmenopausal women.
Study design: Ten controlled clinical trials that included 595 subjects (aged 42-92 years) met our criteria for inclusion. Changes in femoral neck bone mineral density were examined by 2-way analysis of variance tests with repeated measures on 1 factor.
Results: Across all designs and categories, there was an increase in bone mineral density of 0.73% $\pm$ 5.52% and 0.45% $\pm$ 6.78%, respectively, in the exercise and control subjects. However, comparison of initial and final bone mineral density values between exercise and control subjects revealed no statistically significant effect of exercise on femoral neck bone mineral density ($P > .05$).
Conclusion: Collectively, the exercise protocols that were used in this individual patient data meta-analysis do not improve femoral neck bone mineral density in postmenopausal women.

Osteoporosis is a major public health problem in the United States. In 1996, it was estimated that approximately 29 million women and men >50 years old had osteoporosis or had low bone mass and were at risk of having the disease.[1] Of these estimated 29 million women and men, most (approximately 23 million) were women. By the year 2015, the prevalence and risk for this disease among women $\geq$50 years old is estimated to increase to approximately 35 million.[1] The most devastating consequence of osteoporosis and osteopenia is an increased risk for fracture. For example, beginning at age 50 years, white women, which is the group at the greatest risk for osteoporosis and osteopenia, have a 40% chance of fracturing the spine, hip, or distal radius during their remaining lifetime.[2] In absolute terms, the number of fractures that are associated with osteoporosis has been estimated to be approximately 700,000 at the vertebrae, 300,000 at the hip,

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and 250,000 at the distal forearm.[2] In the United States, the health care system costs that are associated with osteoporotic fractures exceed $13.8 billion annually.[3]

Although the greatest number of fractures occur at the vertebrae, the most devastating fracture in terms of economic costs and mortality rates are fractures of the hip, specifically the proximal femur.[4] For example, each hip fracture in the United States has been estimated to cost approximately $32,000 in total medical expenditures.[3] In addition, the 1-year mortality rate after a hip fracture is approximately 20%.[4] Furthermore, although difficult to assess, limited ambulatory skills and fears about additional fractures may affect the quality of life of individuals who have experienced a fracture.[1] Finally, a woman's risk of a hip fracture is equivalent to her combined risk of having breast, uterine, and ovarian cancer.[2]

A recent consensus statement from the National Institutes of Health Consensus Development Panel on Osteoporosis, Prevention, Diagnosis, and Therapy concluded that, during the later years of life, exercise in the presence of adequate calcium and vitamin D intake has a modest effect on slowing the loss of bone mineral density (BMD).[4] Our previous meta-analytic research that used summary means from eligible studies resulted in improvements in BMD at the femur as a result of site-specific aerobic exercise and progressive resistance exercise in postmenopausal women.[5,6] Unfortunately, because of the small number of summary means from the studies, different assessment sites at the femur (femoral neck, Ward's triangle, trochanter, intertrochanter) had to be combined into 1 summary measure. Consequently, we did not examine the effects of exercise on BMD at the femoral neck, the most common site that is assessed at the femur. An alternative approach for dealing with this issue is to conduct a meta-analysis with individual patient data (IPD) rather than summary means from the studies. To the best of our knowledge, we are not aware of anyone who has attempted to use IPD for the purpose of conducting a meta-analysis on the effects of exercise on BMD at the femoral neck in postmenopausal women. Given the health care consequences of low BMD at the femoral neck in postmenopausal women and the potential benefit of exercise, which is a non-pharmacologic intervention that is available to most people, a need exists to examine the effects of exercise on BMD at the femoral neck in postmenopausal women. Therefore, the purpose of this study was to conduct a meta-analysis with IPD to examine the efficacy of exercise for improving BMD at the femoral neck in postmenopausal women.

Methods

Data sources

Studies for this investigation were extracted from a larger exercise and bone density database in which IPD was available. Briefly, obtainment of IPD was accomplished by sending a cover letter and data request form to study authors by postal mail. Authors who did not respond received a follow-up request approximately 5 weeks after the initial mailing. This study was exempt from Institutional Review Board Approval.

Study selection

Inclusion criteria for this study were (1) randomized and nonrandomized trials that included a comparative nonexercise control group, (2) site-specific loading exercise that lasted a minimum of 16 weeks, (3) postmenopausal women only, (4) journal articles, dissertations, and masters theses that were published in the English language literature, (5) studies that were published between January 1966 and December 1998, (6) BMD (relative value of bone mineral per measured bone area) that was assessed at the femoral neck, and (7) ability to obtain IPD from authors. Exclusion criteria for this study included (1) studies in men or premenopausal women, (2) observational studies, (3) review articles, (4) case reports, (5) comments, (6) letters, (7) nonhuman studies, (8) foreign-language articles, and (9) abstracts from conference meetings. We did not include foreign language articles because of the potential for error in the translation and interpretation of findings. We limited our analysis to BMD at the femoral neck because this is the most common site that is assessed and because of missing data for the other sites (Ward's triangle, trochanter, intertrochanter). For studies in which there were multiple publications (ie, retrieved both the dissertation and refereed journal article), we examined and referenced both to derive the maximum amount of information possible but only included this information as 1 set of data.

Data abstraction

A coding sheet that could hold 94 pieces of information was developed and used in this investigation. In addition, coding instructions that described how to code each item on the coding sheet were developed and used. The 3 major categories of variables that were coded for included study characteristics, subject characteristics, and outcome data. All IPD were abstracted and checked for accuracy by the first author. Blinding of the coder to study information (identity and institutional affiliation of authors and study results) was not performed because it has been shown recently that these procedures have neither a statistically significant nor a clinically important effect on the results.[7]

Statistical analysis

For IPD, means $\pm$ SD were used to describe continuous variables; frequencies and percentages were used for categoric variables. For continuous variables,

independent *t*-tests were used to examine differences in initial characteristics between exercise and control groups; chi-square tests were used for categoric variables. To examine initial and final values for BMD between exercise and control groups, a 2-way analysis of variance (ANOVA) with repeated measures on 1 factor was conducted. The within-subjects or trial factor was the assessment of BMD (initial and final), and the between-subjects or grouping factor was group assignment (exercise or control). Because this was an unbalanced design, a general linear model was used. Before the ANOVA was conducted, Pearson product moment correlations were used to examine for potential covariates to enter into the ANOVA model. This was accomplished by an examination of the association between changes in femoral neck BMD and the following variables: age, height, initial body weight, changes in body weight, initial body mass index (kilogram meters squared), changes in body mass index, percent body fat, changes in percent body fat, initial lean body mass, changes in lean body mass, initial maximum oxygen consumption (milliliters per kilograms^{-1} per minute^{-1}), changes in maximum oxygen consumption (milliliters per kilograms^{-1} per minute^{-1}), age at menarche, years after menopause, cigarette smoking, alcohol consumption, calcium and vitamin D intake, compliance (percentage of exercise sessions attended), length of training in weeks, type of exercise intervention (weight-bearing, non–weight-bearing, weight training), type of BMD assessment (dual-energy x-ray absorptiometry, dual-photon absorptiometry), and study design (randomized vs nonrandomized controlled trial). However, because only initial BMD was associated significantly with changes in BMD ($r = 0.147$; $P = .011$) and this variable was already in the ANOVA model, no covariates were entered into the analysis. In addition, we also conducted ANOVA when limited to women who were at least 8 years after menopause. The alpha level for statistical significance for both the Pearson product moment correlations and ANOVA was set at a probability value of $<.05$.

Because we were not able to retrieve IPD from all eligible studies, we also examined whether our results differed between studies in which IPD were available versus those that were not. To accomplish this, we used the standardized difference effect size, which was calculated from the summary data reported in the studies.[8] This was calculated by subtracting the change outcome in the exercise group from the change outcome in the control group and then dividing by the pooled SD of the exercise and control group.[8] The effect size was then corrected for small-sample bias.[8] If means and SDs were missing, the effect size was calculated from reported test statistics.[9] In general, an effect size of 0.20 is considered a small effect, of 0.50 is considered a moderate effect, and of 0.80 is considered a large effect.[10] An effect size of 0.50, for example, means that the exercise group differed from the control group by five-tenths of a SD in favor of the exercise group. For studies that included >1 group, an effect size was calculated for each group independently of the other. We used the standardized difference effect size versus the original metric (BMD in grams per centimeter squared) so that all eligible studies could be included in the analysis. An ANOVA-like random effects model developed for meta-analytic research was used to compare effect size differences between those studies in which IPD were provided versus those that were not. This was accomplished by examining the between and within group differences for the effect sizes and their variances from each group. The alpha level for statistical significance was set at a probability value of $<.05$.

Results

Study characteristics

Twenty-three studies from 25 publications met our criteria for inclusion.[11-35] The number of publications exceeded the number of studies because we included 2 studies that appeared in the form of both a dissertation[29,33] and refereed journal article.[30,34] From these, IPD was available from 10 studies and 11 publications.[12-16,21,22,27,29,30,32] Thus, we were able to include IPD from approximately 43% of eligible studies. A general description of the studies is shown in Table I. Five of the studies were randomized controlled trials, and 5 studies were controlled trials. The 10 studies included a total of 22 groups (12 exercise, 10 control) and 595 subjects (295 exercise, 300 control) that met our criteria for inclusion. The ages of the subjects ranged from 42 to 92 years in the exercise groups and 46 to 86 years in the control groups. The length of training for the studies ranged from 32 to 104 weeks (mean$\pm$SD, 58 $\pm$ 33 weeks). Ten groups performed weight-bearing exercise; 2 groups performed non–weight-bearing exercise, and 2 other groups performed weight training exercise. Six of the studies used dual-energy x-ray absorptiometry to assess BMD at the femoral neck; the other 4 studies used dual-photon absorptiometry.

Subject characteristics

Initial characteristics of the subjects for continuous variables are shown in Table II. As can be seen, there were no statistically significant differences between exercise and control subjects in relation to age, height, body weight, and vitamin D intake. However, subjects in the exercise groups had significantly higher levels of calcium intake, and the number of years after menopause was greater in the control subjects. Initial characteristics of the subjects for categoric variables are shown in Table III. No statistically significant differences were found

Table I Characteristics of femoral neck BMD studies (grams per centimeter squared) in which IPD were provided or available

Study	Design/Subjects	Exercise Intervention(s)	BMD Assessment
Bloomfield et al[12]	CT that included 17 postmenopausal women who were assigned to either an exercise (n = 7; age, 61.9 ± 2.3 y) or control (n = 10; age, 59.4 ± 9.7 y) group	32 weeks of training performed 3 times weekly for 50 minutes per session (15-minute warm-up, 30 minutes of stationary cycling, 5-minute cool-down) at 60%-80% of maximal heart rate	DPA (Lunar DP3)
Bravo et al[13]	RCT that included 106 osteopenic women who were assigned to either an exercise (n = 44; age, 59.8 ± 5.9 y) or control (n = 62; age, 60.0 ± 6.3 y) group	52 weeks of training performed 3 times weekly for 60-65 minutes per session: 10-minute warm-up, 25 minutes of rapid walking (replaced with aerobic dance once each week), and 15 minutes of bench stepping at 60%-70% of MHRR, followed by 10-15 minutes of resistance exercise	DEXA (Lunar DPX)
Brooke-Wavell et al[14]	RCT that included 77 postmenopausal women who were assigned to either an exercise (n = 38; age, 64.9 ± 3.0 y) or control (n = 39; age, 64.1 ± 3.1 y) group	52 weeks of training that consisted of self-monitored walking 3.5 times per week for 14.8 minutes per day for the first 12 weeks, followed by 20.4 minutes per day of walking, 4.8 days per week, for the remainder of the study	DEXA (Lunar DPX)
Caplan and Ward[15]	CT that included 30 postmenopausal women who were assigned to either an exercise (n = 19; age, 66.4 ± 5.1 y) or control (n = 11; age, 65.4 ± 5.0 y) group	104 weeks of aerobic weight-bearing exercise performed twice weekly for 60 minutes (warm-up, 20-25 minutes of low impact aerobic exercise, 10 minutes of ball games for improved hand-eye coordination, followed by work on floor mats for strength and flexibility, 10 minutes of relaxation; subjects were also asked to exercise on their own once each week so that the pulse would be elevated for at least 20-30 minutes	DPA (Lunar DPA)
Ebrahim et al[16]	RCT that included 91 postmenopausal women who were assigned to either an exercise (n = 46; age, 66.5 ± 8.1 y) or control (n = 45; age, 68.2 ± 7.9 y) group	104 weeks of walking 3 times each week for 40 minutes per session	DEXA (Lunar DPX)
Little[21]	CT that included 21 postmenopausal women who were assigned to a resistance training (n = 6; age, 59.3 ± 2.4 y), walking (n = 6; age, 52.2 ± 4.5 y), swimming (n = 5; age, 51.4 ± 5.8 y), or control (n = 4; age, 60.5 ± 1.3 y) group	32 weeks of resistance training consisted of 9 exercises that were performed 3 times per week for 1 set of 8-12 repetitions at 60%-80% of 1RM; walking consisted of 32 weeks of training, 3 times each week for 30-50 minutes per session (5-10 minute warm-up; walking for 20-30 minutes; 5-10 minute cool-down) at 70%-90% of maximal heart rate; swimming consisted of 32 weeks of training, 3 times each week for 30-50 minutes per session (5-10 minute warm-up; walking for 20-30 minutes; 5-10 minute cool-down) at 70%-90% of maximal heart rate-13 beats-per minute	DPA (Lunar)

The number of subjects was limited to those in which valid IPD were available; the groups that were included were limited to those that met our inclusion criteria. *CT*, controlled trial; *DPA*, dual-photon absorptiometry; *RCT*, randomized controlled trial; *MHRR*, maximum heart rate reserve; *DEXA*, dual-energy x-ray absorptiometry; *1RM*, repetition maximum; VO_{2max}, maximum volume of oxygen utilization.

Table I (*Continued*)

Study	Design/Subjects	Exercise Intervention(s)	BMD Assessment
Lord et al[22]	RCT that included 136 subjects who were assigned to either an exercise (n = 66; age, 70.9 ± 5.0 y) or control (n = 70; age, 71.0 ± 5.0 y) group	42 weeks of exercise performed twice weekly for approximately 60 minutes per session (5-minute warm-up, 35-40 minutes of aerobic exercises that consisted of activities for balance, hand-eye and foot-eye coordination, and strengthening exercises, 15 minutes of stretching, and 5-10 minute cool-down)	DEXA (Lunar DPX) (Lunar Corporation, Madison, WI)
Prince et al[27]	RCT that included 61 postmenopausal women who were assigned to a either a calcium and exercise (n = 26; age, 63.6 ± 4.5 y) or calcium (n = 35; age, 62.4 ± 4.8 y) group	104 weeks of weight-bearing exercise performed twice weekly for approximately 60 minutes per session; subjects were also asked to walk another 2 hours per week at 60% of peak heart rate for their age	DEXA (QDR-1000) (Hologic, Inc, Bedford, MA)
Pruitt et al[29,30]	CT that included 26 postmenopausal women who were assigned to either an exercise (n = 17; age, 53.6 ± 4.1 y) or control (n = 9; age, 55.6 ± 2.9 y) group	36 weeks of strength training that consisted of 13 exercises performed 3 times weekly at 50%-60% of 1RM for 1 set of 10-12 repetitions for the upper body and 10-15 repetitions for the lower body	DPA (Lunar DP3) (Lunar Corporation)
Ryan et al[32]	CT that included 30 postmenopausal women who were assigned to either a weight loss (n = 15; age, 62.5 ± 5.5 y) or exercise + weight loss (n = 15; age, 63.4 ± 5.7 y) group	24 weeks of aerobic exercise (treadmill jogging) performed 3 times weekly for up to 35 minutes per session at 50% to >70% of VO_{2max}; each session included a 10-minute warm-up and cool-down period	DEXA (Lunar) (Lunar Corporation)

The number of subjects was limited to those in which valid IPD were available; the groups that were included were limited to those that met our inclusion criteria. *CT*, controlled trial; *DPA*, dual-photon absorptiometry; *RCT*, randomized controlled trial; *MHRR*, maximum heart rate reserve; *DEXA*, dual-energy x-ray absorptiometry; *1RM*, repetition maximum; *VO_{2max}*, maximum volume of oxygen utilization.

between exercise and control groups in relation to cigarette smoking, alcohol consumption, use of estrogen and/or progesterone, previous fractures at any site, and race. Most subjects were not smokers, were not taking any type of estrogen and/or progesterone, and were white. A little more than one half of the subjects reported consuming alcohol and/or experiencing a previous fracture at ≥1 site in the body.

Outcomes

Femoral neck BMD values are shown in Table IV. Across all designs and categories, there was an increase of 0.51% in the exercise subjects and 0.13% in the control subjects.

Comparison of initial and final BMD values for potential differences is shown in Table V. Across all studies and subjects, statistically significant main effect differences were observed for group but not trial. However, there was no statistically significant interaction between group and trial, which indicated that exercise did not have any effect on femoral neck BMD. In addition, no statistically significant interaction was observed when results were analyzed with each study deleted from the model. Furthermore, no statistically significant within or between-group differences in femoral neck BMD were observed when we compared effect size results for studies in which IPD were available with those studies in which these results were not available (IPD available, 0.098 ± 0.352 g/cm^2; IPD not available, 0.164 ± 0.416 g/cm^2; within group difference, 30.725, P = .429; between group difference, 0.242, P = .623).

When ANOVA was conducted and limited to women who were at least 8 years postmenopause, there was a 0.89% increase in femoral neck BMD in the exercise groups (0.007 ± 0.044 g/cm^2) and a −0.58% decrease in the control groups (−0.006 ± 0.060 g/cm^2) . However, all ANOVA results were not significant, including the interaction between initial and final femoral neck BMD values for the exercise and control groups (F [1,195] = 2.69; P = .10).

Comment

The results of this study suggest that exercise does not improve femoral neck BMD in postmenopausal women. In addition, we found no differences between the results of those studies in which IPD were available versus

Table II Initial characteristics of subjects for continuous variables

Variable	N	Exercise*	N	Control*	Significance $t^{\dagger}$ (P value)
Age (y)	278	64.90 ± 7.11	291	65.13 ± 7.12	−0.39 (.70)
Height (cm)	277	159.01 ± 6.69	288	158.42 ± 7.08	1.02 (.31)
Weight (kg)	278	65.54 ± 11.28	286	64.77 ± 12.26	0.77 (.44)
Postmenopause (y)	133	14.37 ± 9.97	127	18.60 ± 10.67	−3.31 (.001)‡
Calcium (mg)	181	946.16 ± 393.60	175	865.43 ± 356.35	2.03 (.04)‡
Vitamin D (IU)	57	198 ± 212	62	161 ± 133	1.17 (.24)

* Data are given as mean ± SD. *N*, number of subjects for whom data were available.
† Independent *t*-test value.
‡ Statistically significant.

Table III Initial characteristics of subjects for categoric variables

Variable	Exercise (n)	Control (n)	χ^2 (P value)
Cigarette smoking	19 (9.0%)	25 (11.4%)	0.71 (.40)
Alcohol consumption	122 (59.5%)	111 (52.9%)	1.87 (.17)
Estrogen/progesterone use	20 (6.9%)	17 (5.9%)	0.28 (.60)
Previous fractures (any site)	58 (52.2%)	63 (57.8%)	0.68 (.41)
Race (white)	213 (99.5%)	214 (98.6%)	0.24 (.63)

Results were limited to studies that reported data for each variable.

Table IV Femoral neck BMD results (g/cm^2)

Group	N	Initial*	Final*	Difference*
Exercise	295	0.787±0.123	0.791±0.124	0.004±0.039
Control	300	0.763±0.122	0.764±0.117	0.001±0.048

* Data are given as mean ± SD.

those in which IPD were not available. Furthermore, our results are consistent with most findings of the original studies in that 79% of the outcomes at the femoral neck were reported as not being statistically significant. In contrast, our findings appear to be somewhat different than the recent position statement from the National Institutes of Health Consensus Development Panel on Osteoporosis, Prevention, Diagnosis, and Therapy, which suggested that exercise during the later years probably has a modest effect on slowing the decline in BMD.[4] However, this was a broad statement and not specific to any 1 site in the body. Our findings also conflict with our previous meta-analytic work in which an approximate 2% improvement in BMD was found at the hip as a result of site-specific aerobic exercise and progressive resistance training.[5,6] One of the possible reasons for the discrepant results between our current and previous meta-analytic work may have to do with the fact that the summary measures that were obtained in our previous research were the result of pooling the outcomes from all sites that were assessed at the femur (femoral neck, Ward's triangle, trochanter, intertrochanter). Consequently, it may be that improvements in BMD occur at sites other than the femoral neck (Ward's triangle, trochanter, intertrochanter). However, we were unable to address the effect of exercise on the other BMD sites at the femur in this investigation.

It has been reported that calcium and vitamin D supplementation during the early postmenopausal years does not improve BMD, although modest improvements are observed during the later postmenopausal years. Although we did not find a statistically significant effect as a result of exercise training, we did observe a trend ($P = .10$) for such improvements.[36] Given our findings, it would appear plausible to suggest that additional large, well-designed randomized controlled exercise trials on this topic be conducted to address this issue.

The recent consensus statement from the National Institutes of Health Consensus Development Panel on Osteoporosis, Prevention, Diagnosis, and Therapy suggested that higher impact activities and resistance training may have the greatest effect on BMD.[4] However, as can be seen in Table I, most of the studies that were included in this investigation used lower versus higher impact types of activities, primarily walking, as an intervention. In addition, although exercises that were designed to strengthen the hip were used in studies that used a progressive resistance training protocol, most exercises focused on movements that were designed to strengthen the upper body. Thus, it may be that the lack of improvement in femoral neck BMD in this investigation was the result of the exercise protocols that were used. However, although higher impact activities (such as jumping and high impact aerobic dance) may be more beneficial to femoral neck BMD,[37,38] this has to be countered with issues of adherence to a regular program of exercise and the potential to put the subject at

Table V ANOVA summary table for femoral neck BMD (general linear model)

Source of variation	Degrees of freedom	Sum of squares	Mean square	F-ratio	*P* value
Group (exercise and control)	1	0.193	0.193	6.730	.010*
Subjects (group)	593	16.991	0.0287	—	—
Trial (initial and final BMD)	1	0.00217	0.00217	2.277	.132
Group × trial	1	0.000816	0.000816	0.857	.355
Residual	593	.565	0.000952	—	—
Total	1189	17.752	0.0149	—	—

* Statistically significant.

an increased risk for injury, particularly stress factures and osteoarthritis.[39] Thus, from a practical standpoint, the lower impact types of exercise protocols that were used in many of our included studies are probably the most appropriate. This may be true especially for walking because it is the most common type of exercise in which people in the United States participate.[40]

Because the terms lower and higher impact are broad and fairly subjective terms, it would appear plausible to suggest that future studies that examine the effects of exercise on BMD make some attempt to quantify the forces that are involved for the interventions used. For those studies that use a progressive resistance training protocol, additional lower leg exercises that may affect femoral neck BMD should be used. The incorporation of these suggestions should result in a better understanding regarding the efficacy of exercise for the improvement of BMD at the femoral neck.

Despite the fact that exercise did not have any effect on femoral neck BMD, such activities should almost always be recommended. For example, although exercise may not improve femoral neck BMD, it may increase muscular strength and balance and improve postural stability, thus reducing the risk of falling and the subsequent fractures that can result from falling.[4,41] Although it is important for future research to examine the efficacy and effectiveness of various exercise interventions on femoral neck BMD, it would appear reasonable to suggest that a need exists for increased research that addresses the effects of exercise for the prevention of osteoporotic fractures in the presence and/or absence of changes in BMD.

Although the use of the meta-analytic approach provides for a more objective evaluation of studies when compared with the traditional narrative review, limitations do exist. In general, the very nature of meta-analysis dictates that the meta-analysis itself inherits the limitations that exist in the literature. As a result, the application of results across all types of subjects meeting the inclusion criteria for a meta-analysis may not be appropriate. This is important to remember for clinicians who include meta-analyses in the decision-making process. In addition, one of the most common problems in meta-analysis is missing data. For example, in this study, we were unable to retrieve all of the IPD that met our inclusion criteria. Although we found no statistically significant difference in femoral neck BMD among studies that provided IPD versus those studies that did not, our null results may have been the consequence of being underpowered to detect a statistically significant difference because of the inability to retrieve a larger percentage of IPD.

In conclusion, the results of this study suggest that exercise does not improve femoral neck BMD in postmenopausal women.

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APPENDIX E
Published Abstracts of Presentations at Professional Conferences

Medicine & Science in Sports & Exercise: Volume 31(5) Supplement May 1999 p S249

COMMON METRIC VERSUS STANDARDIZED DIFFERENCE FOR META-ANALYSIS OF BONE DENSITY STUDIES
[Annual Meeting Abstracts]

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Abstract 1189

The purpose of this study was to compare the use of the common metric versus standardized difference effect size for pooling results from a sample of controlled trials examining the effects of exercise on bone density at the hip in postmenopausal women. The most commonly reported metric (percent change) was compared to the standardized difference effect size. A total of 13 values were included in the analysis. Using a fixed-effects model, common metric (CM+) effect size showed an increase of 0.36 percent (95 percent confidence interval = -0.09 to 0.81). From a clinical standpoint, this is considered a "small" effect. The standardized approach (STD+) showed an average effect of 0.20 (95 percent confidence interval = 0.02 to 0.38). This is also considered a "small" effect. No significant heterogeneity (Q) was observed for either common metric or standardized results (common metric, Q = 18.80, p = 0.09, standardized difference, Q = 13.61, p = 0.33). For this set of studies, the use of either the most commonly reported metric (percent change) or the standardized effect size produced similar results. This is evidence to support recommending the use of the commonly reported metric when studies included in a meta-analysis report outcomes in the same metric. For clinicians and researchers, use of the common metric will be more clinically meaningful and will enhance interpretation of results for a wider range of readers. Supported by U.S. Department of Defense DAMD17-8513

Section Description

American College of Sports Medicine; 46th Annual Meeting; Washington State; Convention & Trade Center; June 2-5, 1999

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E-26 POSTER BONE DENSITY & EXERCISE

ferred aerobic intensity, both water aerobics and treadmill running are of similar exercise intensity. Furthermore, during self-paced exercise, both of these activities met the ACSM guidelines for the development and maintenance of cardiorespiratory fitness.

Psychometric Properties of a Revised Scale of Attributes of Fitness Services

Mandy M. Huset, Dean F. Anderson, and Galen T. Trail, Iowa State University

Despite the rising importance of customer satisfaction, many corporations and businesses still lack efficient methods for defining and meeting customer needs. One industry in particular that needs to direct more attention towards the importance of customer satisfaction due to increased market competition is the health and fitness industry. A valid and reliable scale is necessary to measure customer satisfaction with fitness services. This investigation examined the psychometric properties of a revised Scale of Attributes of Fitness Services (SAFS). Data were collected from 307 participants in three fitness programs. Among 307 respondents, 21% were from a university exercise clinic (n = 63), 56% were from a commercial fitness club (n = 172), and 23% were from a community park and recreation wellness center (n = 71%). For the total sample, 95% of the respondents self-identified as Caucasian, and 69% were female. Average age was 48 years with a range of 17 to 83 years. In addition, 84% of the respondents indicated that they had been exercising at least 20 min a day, 3 days per week, for 6 months or longer. The revised SAFS consisted of 63 items measuring 13 different fitness service components; each represented with at least three items. A 7-point Likert-type scale from 1 (not at all satisfied or not at all important) to 7 (very satisfied or very important) was utilized to measure both satisfaction ratings and importance ratings of items. Internal consistency was examined using Cronbach's alpha for each of the subscales. The 13 importance subscale coefficients ranged from .66 to .86 and the 13 satisfaction subscale coefficients ranged from .56 to .91. Only two subscales, core consumer importance (.66) and core consumer satisfaction (.56) displayed coefficients below the .70 standard recommended by Nunnaly (1978). A confirmatory factor analysis for the importance items showed fair fit for the model with a RMSEA of .071 and only 9% of the residuals were greater than the recommended standard of .10 (Bagozzi and Yi, 1988) suggesting a fair model fit. The CFA for the satisfaction items showed similar results. Once again, the RMSEA showed a moderate fit at .067 and only 6.6% of the residuals for satisfaction items were greater than the .10 standard. Thus, the results suggested reasonable validity and reliability levels for the subscales and items with the exception of only the consumer core importance and satisfaction subscales.

Effect of Music Tempo on Heart Rate and Perceived Exertion During Rest, Exercise, and Recovery

Stephanie M. Jensen, Holly D. Cram, and Bruce L. Van Duser, Gustavus Adolphus College

Many feel that it is beneficial to exercise while listening to music. Northrup (1998) documented that music affects our emotions, moods, and performances. The purpose of this study was to examine the effects of music on heart rate (HR) and perceived exertion (PE) at rest, exercise, and exercise recovery. Ten college women participated in this study. A repeated measures design compared differences in HR and PE during no, slow, and fast music conditions at rest and low, moderate, and high level exercise, and recovery. The sequence of music conditions was randomized. Treadmill exercise consisted of 3-min stages at zero percent grade and two mph, five percent grade and three mph, and ten percent grade and five mph. Recovery consisted of zero percent grade at two mph. A repeated measure ANOVA revealed that heart rate was significantly higher for the fast music condition compared to the no music condition at rest and during low-level exercise ($p < .05$). There were no significant differences ($p > .05$) in PE. The results of this study indicate that music tempo does influence heart rate and that exercising to fast music may not be as effective during submaximal work as exercising to other music tempos.

Resistance Training and Bone Mineral Density in Women: A Meta-Analysis of Controlled Trials

George A. Kelley and Kristi S. Kelley, Northern Illinois University, and Zung Vu Tran, University of Colorado

It is estimated that approximately 26.2 million white, postmenopausal women in the United States have either osteopenia or osteoporosis (Melton, 1995). Recent meta-analytic work has demonstrated the positive effects of aerobic, weight bearing exercise on bone mineral density (BMD) in postmenopausal women (Kelley, 1998). Unfortunately, studies examining the effects of resistance exercise on BMD in adults have led to less than positive results. The purpose of this study was to use the meta-analytic approach to examine the effects of resistance training on BMD in women. Studies were retrieved via (a) computerized databases (MEDLINE, Current Contents, Sport Discus, Dissertation Abstracts International), (b) reviewing the reference lists from both original and review articles, (c) hand searching selected journals, and (d) consultation with experts (Charlotte Sanborn, David Nichols, and Christine Snow). Twenty-nine studies that included a total of 94 effects sizes (femur = 53, lumbar spine = 24, radius = 17) in 572 exercise and 551 control participants met the criteria for inclusion. Using a fixed-effects model because of a lack of statistically significant heterogeneity at all sites, overall outcomes resulted in small, but statistically significant effect size changes at the lumbar spine (lumbar spine, $M \pm SD = 0.24 \pm 0.36$, 95% BCI = 0.11 to 0.38). Changes in lumbar spine BMD were equivalent to a 0.19% decrease in the exercise group and a 1.45% decrease in the control group. Subgroup analyses demonstrated that only postmenopausal women had an improved BMD profile at the femur and radius sites after resistance training (femur, $M \pm SD = 0.15 \pm 0.38$, 95% BCI = 0.03 to 0.28; radius $M \pm SD = 0.52 \pm 0.36$, 95% BCI = 0.33 to 0.71). Changes were equivalent to a 0.40% increase at the femur in the exercise groups and a 0.21% decrease in the control groups. At the radius site, a 1.71% increase was observed in the exercise groups and a 1.39% decrease in the controls. The results of this meta-analysis suggest that resistance training has a positive effect on the BMD of all women

at the lumbar spine, and in postmenopausal women at the femur and radius.

This study was funded by the United States Department of Defense, Army Medical Research and Material Command Award #17-98-1-8513.

Immune Function in Elite Teenage Tennis Athletes

M. W. Kernodle, D. C. Nieman, D. A. Henson, Appalachian State University, and G. Sonnenfeld, Morehouse School of Medicine

This study had two objectives: (a) To investigate the chronic response of the immune system to training by teenage tennis athletes; (b) To study the influence of carbohydrate supplementation on the acute hormonal and immune response to 2 hr of intensive tennis drills. Resting immune function was compared in 20 elite teenage tennis athletes recruited from the Van Der Meer Tennis Center in Hilton Head, and 18 matched nonathletic controls. Blood concentrations of leukocyte subsets did not differ between athletes and controls except for a slight decrease (16%) in the neutrophil count among the athletes (3.38 ± 0.17 and 4.03 ± 0.24 10^3 cells/L, respectively, $p = .03$), and a 53% elevation in the natural killer (NK) cell count (0.58 ± 0.06 and 0.38 ± 0.05 10^3 cells/L, respectively, $p = .02$). Salivary IgA output, and two measures of T cell function did not differ between groups. Infection logs (March 1–May 14) revealed no difference in the number of days sick with upper respiratory tract infections (URTI) among athletes and controls (4.2±0.9 and 6.6 ± 1.7 days, respectively, $p = .226$). In general, these data indicate that despite intensive training by tennis athletes (17.6 ± 1.4 hr/week), immune function and incidence of URTI was normal. The elevation in NK cell count is consistent with previous studies in athletes who tend to have an enhanced recirculation and activity of NK cells. In phase two of this study, the influence of carbohydrate versus placebo beverage consumption on immune and hormonal responses to 2 hr of tennis drills was measured (randomized, double-blind, placebo-controlled) in the 20 elite tennis athletes. Three blood samples were collected [pre-exercise (6:30–7:00 a.m.), immediately postexercise (9:30 a.m.), and 1-hr postexercise (10:30 a.m.)]. Following the pre-exercise blood draw, athletes ingested 650 ml of a 6% carbohydrate or placebo beverage. At 7:30 am, athletes began an intensive 2-hr bout of tennis drills, while ingesting 160 ml carbohydrate or placebo every 15 min. Athletes trained at a pace that elicited a heart rate of 159 ± 4 beats/min (81 ± 2.4% maximum heart rate) and an RPE of 12.8 ± 0.8 or "somewhat hard"). Carbohydrate versus placebo ingestion had no influence on patterns of immune or hormonal changes following exercise. Leukocyte and lymphocyte subset changes following exercise were moderate, with the neutrophil/lymphocyte ratio rising from 1.39 ± 0.08 to 2.54 ± 0.27 postexercise, and 2.73 ± 0.33 1-hr postexercise. Salivary IgA output decreased moderately (30%) postexercise before returning to normal 1 hr postexercise. Interleukin-2 production and mitogen-induced lymphocyte proliferation (two measures of T cell function) were unchanged following exercise, and cortisol was not elevated. These data indicate that a 2-hr exercise bout of tennis drills is associated with a mild perturbation of immunity which is unaffected by carbohydrate ingestion.

Acute Effects of Stretching Are Not Evident in the Kinematics of the Vertical Jump

Duane Knudson, Kati Bennett, Rod Corn, David Leick, and Chris Smith, California State University–Chico

Stretching during warm-up for physical activity is common practice despite recent studies showing decreased isometric and dynamic strength performance following stretching. Initial studies into the mechanism of this phenomenon are inconclusive. The purpose of this study was to document changes in kinematic variables related to stretch-shortening cycle (SSC) performance in vertical jumps following two warm-up protocols, stretching (S) and control (S). Ten male and 10 female young adults gave informed consent and were tested at the same time of the day a week apart with the warm-up order selected at random. Reflective markers defining a four segment biomechanical model were taped to participants followed by a 3-min ride (80 rpm) on a Lifecycle. In the C protocol participants sat for 10 min. The S protocol consisted of three 15-s static stretches of the hamstrings, quadriceps, and calf muscles. Participants then performed three maximal effort vertical jumps with hands on hips. Sagittal plane video (60 Hz) of the jumps was recorded, and Peak Performance Technologies hardware and software were used to calculate four dependent variables related to SSC performance: peak vertical velocity (V_p), smallest knee angle (θ_K), and durations of the eccentric (t_E) and concentric (t_C) phases. The mean of three jumps was used for statistical analysis using a multivariate analysis of variance (MANOVA) with repeated measures. Main effects for each dependent variable were examined by dependent *t* tests. Statistical significance was accepted at the .05 level. MANOVA demonstrated a nonsignificant, $F(1, 19) = 1.39$, $p = .25$, effect of S on the dependent variables. There was a nonsignificant, $t(1, 19) = -1.59$, $p = .13$, trend of a 3% smaller V_p following S compared to C. The effect of S was not uniform across participants with 55% showing a decrease in V_p (7.5%) after S and 45% showing no change or an increase in V_p (2.4%) after S. The changes in V_p were not related to jumping ability, and the magnitude of these changes was consistent (4-8%) with recent research on performance decrements following stretching. The nonsignificant differences in the kinematic variables of jumping are not likely Type II errors, because statistical power for all variables except t_E was greater than 0.85 for detecting a true difference of 5%. The mechanism of acute decreases in jumping for most performers from stretching requires further study.

Prediction of One-Repetition Maximum (1-RM) Strength in Large Muscle Groups From a 4–6 RM and a 7–10 RM Submaximal Strength Test in Healthy Young Adult Men

Derek Lemire, Ben R. Abadie, and Clay Daughtrey, Mississippi State University

Many investigators have produced regression equations to predict 1-RM strength from a 7–10 RM submaximal strength test. The purpose of this investigation was to determine if 1-RM strength could be predicted from a 4–6 RM submaximal strength test with a higher accuracy than the commonly employed 7–10 submaximal strength test. Thirty-four healthy men between the ages of 19 and 32 years participated in this study. Participants were instructed not to participate in strenuous

298 BONE MINERAL DENSITY IN HIGH LEVEL MALE ATHLETES OF DIFFERENT SPORTS - EFFECTS OF SPECIFIC TRAINING AND MUSCLE STRENGTH

P. Platen, E.-H.-Chae, R. Antz, H. Lehmann, J. Kühlmorgen, B. Alloiio
Inst. of Sports Medicine, German Sports University, Cologne

The purpose of the study was to determine bone mineral density (BMD) at the lumbar spine (LSP) and femoral sides (FEM) in top athletes of different sports and untrained controls and to estimate the influences of muscle strength, training-specific and anthropometric parameters on BMD. BMD was measured via DXA in 173 males between 18 and 31 yrs (104 athletes: runners (R, n=21), cyclists (C, n=12), triathletes (TRI, n=18), heavy athletes (HA, judo and wrestling, n=28), and team sport athletes (TS, handball, soccer, basketball, volleyball, n=25), 44 unspecifically trained sport students (STU) and 25 untrained controls (UT). Strength was determined as strength of back extension, hip abd- and adduction, and grip strength. Sport-and group-specific differences in anthropometric but not in strength parameters were found. Marked sport- and group-specific differences were found for BMD values at LSP and the femoral sides (values are in g/cm2): HA: 1.36, 1.21, 1.01, 1.43, 1.10: TS:1.28, 1.17, 1.01, 1.46, 1.04; STU: 1.22, 1.08, 0.96, 1.37, 0.95; R: 1.10, 1.05, 0.91, 1.36, 0.93; TRI: 1.08, 1.03, 0.88, 1.31, 0.92;C: 1.09, 0.95, 0.84, 1.20, 0.84, UT: 1.09, 0.91, 0.81, 1.23, 0.78; for BMD values at LSP, NECK, TROCH, INTER, and WARDs, respectively. Group (G) specific effects on BMD got clearest when calculating the percentual differences between BMD values of the athletes and UT. Multiple regression analysis revealed lean body mass to be the strongest predictor for BMD at LSP and FEM. We conclude, that mechanical loads have strong effects on bone adaptation. Sport-specific and region-specific effects, however, have to be taken into account when intending bone adaptations. Not training quantity but quality is important for high osteogenic effects. Dynamic sports with short, high, and multidimensional loads and partly unphysiological movements have the highest osteogenic effects.

299 CORRELATIONS BETWEEN BONE MINERAL DENSITY, CORION THICKNESS, AND ULTRASOUND VELOCITY IN HIGHLY TRAINED MALE ATHLETES

E.-H. Chae, P. Platen, R. Antz, H. Lehmann, J. Kühlmorgen, B. Alloiio
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The purpose of the study was to determine bone mineral density (BMD) at the lumbar spine (LSP) and femoral sides (FEM) in top athletes of different sports and untrained controls and to analyse validity of methods without radiation exposure for the determination of BMD in young and healthy sportive males. BMD was measured via DEXA in 173 males between 18 and 31 yrs (104 athletes: runners (R, n=21), cyclists (C, n=12), triathletes (TRI, n=18), heavy athletes (HA, judo and wrestling, n=28), and team sport athletes (TS, handball, soccer, basketball, volleyball, n=25), 44 unspecifically trained sport students (STU) and 25 untrained controls (UT). BMD values were compared to corium thickness at the upper left arm (measured by ultrasound) and ultrasound transmission velocities (UTV) at the calcaneus and patella. Marked sport- and group-specific differences were found for BMD values at LSP and the femoral sides (values are in g/cm2). Corium thickness was highest in HA compared to all other groups, who did not differ significantly among each other. UTV at the patella was higher in TS compared to all other groups. UTV at the calcaneus revealed more sport-specific differences with high values in C and TS. Only slight correlations existed between BMD values and corium thickness. Few correlations could be detected between BMD at FEM and UTV at the patella, while BMD at LSP was not all correlated to UTV at the patella. UTV at the calcaneus showed no correlations al all to any BMD value. We conclude that in bony adaptation, sport-specific and region-specific effects have to be taken into account. Measurement of corium thickness is not a suitable method for the estimation of BMD in young and healthy males. Measurement of UTV, however, seems to be valuable for the analysis of region- and load-specific effects on bone, however, due to region-specific effects of physical loads, is not appropriate to calculate BMD at LSP and FEM.

300 EXERCISE AND BONE MINERAL DENSITY IN MEN: A META-ANALYSIS

G.A. Kelley, FACSM, K.S. Kelley, Z.V. Tran, FACSM. Northern Illinois University, De Kalb, IL

Osteoporosis and low bone mass are major public health problems affecting approximately 5 million men aged 50 years and older in the United States. The purpose of this study was to use the meta-analytic approach to examine the effects of exercise on bone mineral density (BMD) in men. Studies were retrieved via (1) computer searches (MEDLINE, Current Contents, Sport Discus, Dissertation Abstracts International), (2) cross-referencing from review and original articles, and (3) consulting experts in the field of exercise and bone density. Inclusion criteria were as follows: (1) randomized or nonrandomized controlled trials, (2) exercise as the only intervention, (3) adult male humans, (4) journal articles, dissertations, and masters theses published in the English-language literature, (5)studies published between January 1966 and December 1998, (6) BMD assessed, (7) training studies lasting a minimum of 16 weeks. Effects sizes (ES) were calculated using the standardized difference approach. Twenty-six ESs representing 225 subjects from eight studies met the criteria for inclusion. Statistically significant exercise-induced increases in BMD were found when the sites assessed were specific to the sites loaded (ES = 0.213, 95 percent bootstrap confidence interval, 0.007 to 0.452). Changes corresponded to increases of approximately 2.6 percent (exercisers, 2.1 percent, controls, -0.5 percent). Statistically significant changes were found for older (greater than 31 years) versus younger (less than 31 years) adults, with differences between groups statistically significant (p=0.04). For older adults, changes were statistically significant at the femur, lumbar, and os calcis sites. The results of this study suggest that site-specific exercise may help to improve and maintain BMD at the femur, lumbar, and os calcis sites in older men. However, the biologic importance of the small changes observed for most outcomes as well as the quality of studies prevents us from forming any firm conclusions regarding the use of exercise for maintaining and improving BMD in men. Clearly, a need exists for additional studies.

301 HIGHER CALCIUM ABSORPTION RATES AND CIRCULATING CALCITRIOL LEVELS IN EXERCISE-TRAINED YOUNG MEN COMPARED TO SEDENTARY CONTROL SUBJECTS

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The effect of physical activity on human calcium (Ca) metabolism is still not completely understood. Therefore, we investigated fractional Ca absorption, by means of a stable strontium test (Fc240), 25-hydroxyvitamin D, calcitriol and renal Ca excretion in young men (n=31) with a high level of sport activity (15.0°6.6 h per week, designated as athletes, and in a group (n=26) of age-matched sedentary control subjects (sport activity 1.0°1.4 h per week, designated as controls). Energy intake (4 day food record) was 40% higher ($P<0.001$) and dietary Ca intake was approximately 100% higher ($P<0.001$) in the athletes compared to the controls. Athletes had significantly higher serum calcitriol levels and Fc240 values than controls ($P<0.001$ and $P<0.01$, respectively). In a stepwise multiple regression analysis including serum levels of 25-hydroxyvitamin D, calcitriol, testosterone and dietary Ca intake only calcitriol was significantly correlated with Fc240 ($p=0.017$). Daily urinary Ca excretion was only slightly higher in the athletes compared to the controls ($p<0.05$). However, additional Ca losses might have occurred through the sweating during sport activities, as indicated by a difference of 1,7 liter between fluid intake and renal fluid excretion ($P<0.001$) in the athletes. In summary, physical active young men have higher fractional Ca absorption rates in comparison to sedentary controls. This alteration is most probably mediated by calcitriol. An additional Ca retention might, however, only be obtained if absorbed Ca exceed total obligatory Ca losses.

B-23C FREE COMMUNICATION/POSTER CARDIOPULMONARY REHABILITATION

302 CORONARY RISK FACTORS AND QUALITY OF LIFE IN CARDIAC PATIENTS AFTER MYOCARDIAL INFARCTION: A COMPARISON OF CHANGES FOLLOWING THREE DIFFERENT TREATMENT APPROACHES

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(Sponsor: R. Pate, FACSM)

This study intended to analyze the effects of different physical activity patterns on patients who experienced acute myocardial infarction, observing eventual changes in symptoms, risk factors (RF), and health-related quality of life (HRQL). Three groups with conventional clinical treatment were formed retrospectively for this study: Group I - supervised exercise in cycloergometer, five times a week, 40 minutes per session, plus muscular endurance and stretching exercises for 15 minutes); Group II, spontaneous physical activity; and Group III, with conventional clinical treatment only (no regular physical activity reported).Observed risk factors included: blood pressure, total cholesterol (TC), HDL-C, LDL-C, triglycerides glycemia, and smoking. HRQL was assessed by a questionnaire developed by Oldridge(1998). A protocol was established to obtain data from a group of 45 patients living in Florianopolis, SC (Brazil), 15 registered in a Clinic (Cardiosport - Group I), and 30 from the Institute od Cardiology at the Regional Hospital (Groups II and III). Subjects in Groups II and III were selected from a list of over 300 patients observing the diagnosis, clinical data, family history, sex, smoking status, and age, all matched with Group I. Data collected from the files also included personal and anthropometric information, educational level, presence of risk factors (dependent variables) at the beginning of the treatment and six months later. Descriptive statistics, one-way ANOVA, and Chi-square were utilized to analyze the data. Results indicate significant ($p<0.05$) modification in risk factors (smoking, TC, HDL-C, LDL-C, HDL/TC, triglycerides, waist/hip circunference, and blood pressure) greater in Group I when compared with Groups II and III. Group I had a reduction in medication and symptoms, while groups II, and mostly Group III, increased medication after the six-month follow-up. Results for HRQL followed the same trend, showing better perception of weel-being in Group I.

303 HIGH VERSUS LOW INTENSITY HOME-BASED CARDIAC REHABILITATION PROGRAMS IN OLDER CORONARY PATIENTS

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Physical activity produces physiological and psychological improvements in cardiovascular disease risk factors and secondary prevention programs. However, there is limited evidence regarding the effectiveness of home-based exercise cardiac rehabilitation (CR) programs in older adults. Specifically, exercise intensity has not been determined in this group or setting. We evaluated the effects of exercise intensity in home-based CR programs for older (>65 years) sedentary patients. The study population included thirty men and women (mean age 78 ± 5 years, 83% female) randomly assigned stepwise into three groups. The high (HI) intensity group (65-70% HR_{max}) received a home exercise program of progressive walking; the low (LOW) intensity group (<60% HR_{max}) received a home program of light calisthenics exercises; and the CONTROL group received only routine care, no exercise program was prescribed. Peak oxygen consumption (VO_{2peak}) was predicted by a step test in the home and measured by a symptom-limited treadmill test in the laboratory; cardiac exercise self-efficacy (CESEI) and quality of life (SF-36) were scored before and after the 16-week conditioning program. Post-training, the HI group (n=8) showed significant increases in VO_{2peak}, self-efficacy and quality of life outcome measures; the LOW group (n=5) significantly improved self-efficacy and quality of life scores; and the CONTROL group (n=8) remained constant. Step and treadmill tests yielded equivalent measures of VO_{2peak}. Home-based training appears to be safe and dose-dependent to result in significant increases in VO_{2peak}, CESEI and SF-36 in older coronary patients. Supported by the Doris Alma Mary Anderson Fund

4270.0: Tuesday, October 23, 2001 - Board 8

Abstract #21099

Aerobic exercise and bone mineral density in women: A meta-analysis

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OBJECTIVE: Examine the effects of aerobic exercise on bone mineral density (BMD) in women. **METHODS:** Meta-analysis of studies that met the following inclusion criteria: (1) randomized or nonrandomized controlled trials, (2) aerobic exercise as the only intervention, (3) adult female humans ages 18 years or older, (4) journal articles, dissertations, and masters theses published in the English-language literature, (5) studies published and indexed between January 1966 and December 1998, (6) BMD assessed at the femur, lumbar spine, or radius, (7) training studies lasting at least 16 weeks. **RESULTS:** Twenty-four studies representing 58 groups (31 exercise, 27 control) and 1,029 subjects (517 exercise, 512 control) met the criteria for inclusion. Using a random-effects model, small but statistically significant effect size changes in BMD were observed at the lumbar spine (mean ± SD=0.33 ± 0.49, 95% confidence interval=0.16 to 0.50) and femur (mean ± SD=0.25 ± 0.35, 95% confidence interval=0.14 to 0.35). Changes in lumbar spine BMD were equivalent to a 0.37% increase in the exercise groups and a 1.87% decrease in the control groups. For the femur, changes were equivalent to 1.37% increase in the exercise groups and a 0.58% decrease in the control groups. No statistically significant changes were observed at the radius (mean ± SD=0.10 ± 0.45, 95% confidence interval=-0.20 to 0.41). **CONCLUSION:** Aerobic exercise has a small but positive effect on BMD at the lumbar spine and femur in women.

Learning Objectives: At the conclusion of the session, the participant (learner) in this session will be able to: 1. Describe the effects of aerobic exercise on bone mineral density in women. 2. Discuss weaknesses in the aerobic exercise and bone density literature as it pertains to women. 3. Identify areas for future research on the effects of aerobic exercise on bone density in women.

Keywords: Exercise, Preventive Medicine

Presenting author's disclosure statement:
Organization/institution whose products or services will be discussed: None
I do not have any significant financial interest/arrangement or affiliation with any organization/ institution whose products or services are being discussed in this session.

The 130th Annual Meeting of APHA

5027.0: Wednesday, November 13, 2002 - Board 1

Abstract #36418

Exercise and Lumbar Spine Bone Mineral Density in Postmenopausal Women: A Meta-Analysis of Individual Patient Data

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PURPOSE: The purpose of this study was to conduct a meta-analysis of individual patient data (IPD) in order to examine the effects of exercise on lumbar spine bone mineral density (BMD) in postmenopausal women. **METHODS:** IPD were requested from a previously developed database of summary means from randomized and nonrandomized trials dealing with the effects of exercise on BMD. Two-way analysis of variance (ANOVA) tests with pairwise comparisons ($p < 0.05$) and 95% confidence intervals (CIs) were used to determine the statistical significance for changes in lumbar spine BMD. **RESULTS:** Across 13 trials that included 699 subjects (355 exercise, 344 control), a statistically significant interaction was found between test and group ($F=15.232$, $p=0.000$). Pairwise comparisons (Bonferroni t-tests) revealed a statistically significant increase in final minus initial BMD for the exercise group (mean +/- SD=0.005 +/- 0.043 g/cm^2, $t=2.46$, $p=0.014$, 95% CI=0.001 to 0.009) and a statistically significant decrease in final minus initial BMD for the control group (mean +/- SD=-0.007 +/- 0.045 g/cm^2, $t=-3.051$, $p=0.002$, 95% CI=-0.012 to –0.002). Changes were equivalent to an approximate 2% benefit in lumbar spine BMD (exercise, +1%, control, -1%). **CONCLUSIONS:** The results of this IPD meta-analysis suggest that exercise helps to improve and maintain lumbar spine BMD in postmenopausal women.

Learning Objectives:

- At the conclusion of this session, the participant (learner) in this session will be able to
  -
  - 1.Describe the effects of exercise on bone mineral density at the lumbar spine in postmenopausal women.
  - 2.List and describe the effects of potential moderators on exercise-induced changes in bone mineral density at the lumbar spine in postmenopausal women.
  - 3.Identify areas of future research for studies dealing with the effects of exercise on bone mineral

density at the lumbar spine in postmenopausal women.

Keywords: Exercise, Women

Presenting author's disclosure statement:
I do not have any significant financial interest/arrangement or affiliation with any organization/ institution whose products or services are being discussed in this session.

Meta-analysis and Methods

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1256 EFFECTS OF HYDROELETROLYTIC RESTORATION ON THE SOLDIERS HYDRATION STATUS DURING THREE DAYS OF MARCH IN AMAZON

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The purpose of this study was to evaluate the effect of three types of hydroeletrolytic restoration strategy associated with alimentation on soldiers' hydration status during three days of military march. Fifty nine male volunteers specialized in jungle operations (20.1 ± 1.97 yr, 168 ± 6.1 cm, 66.5 ± 8.3kg and VO2 max = 51.97 ± 4.91 ml.min-1.kg-1) took part in the study. The subjects were assigned to three groups and performed an approximately 8-hours march through the jungle daily, with a mean temperature of 26.1o ± 1.3o C and relative humidity of 92%, following the same itinerary, but using three different strategies of fluid replacement. An isotonic solution (Sport drink), placebo and water were administered to each group, namely GISO, GPLA and GWAT, respectively. While GISO and GPLA drank 0.5 l/h of fluid during the march, GWAT drank only two canteens (2l), following Brazilian Army jungle water replacement doctrine. From the 3rd to 5th day, before the beginning and after the end of each march, urine specific gravity, body weight, plasmatic proteins, urea concentrations and the haematocrit were measured and verified. During the night all groups were liberated to eat the individual ration and drink water ôad libitum". Factorial ANOVA 3x6 with repeated measures in the second factor or ANCOVA, when the variables were not homogenous at pretest, were used to analyze the data before and after the marches on the three groups. Significant differences ($p < 0.05$) were found in urine density, plasmatic proteins, urea and haematocrit only between GWAT and the others. These differences arose mainly at the third day of march, probably due to the lower fluid ingestion in the GWAT. However, the ôad libitumõ water intake during the night associated with the alimentation seemed not to be sufficient to compensate the loss, underlining the importance of a greater intake of fluids during the march. Although we expected to find significant differences between the GISO and the others groups, because of the long time in which they did not eat during the march, it not occurred. Probably it was due to the facts that the temperature was not high enough, the subjects were acclimatized and/or the marches were not sufficiently intense. Partially supported by Advanced Nutrition

1257 AV3V LESIONS REDUCE SALIVATION AND THERMAL TOLERANCE.

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The anteroventral third ventricular region (AV3V) of the brain is important in the regulation of body fluid balance. Lesions of this area impair tail dilation, water intake, vasopressin release and salivation in response to various stimuli. **PURPOSE:** To determine the influence of the AV3V region on salivation and thermal tolerance during a heat stress. **METHODS:** AV3V and sham lesions were generated in 12 (6 per group) male Sprague-Dawley rats (300-400g). During the following 3 weeks rats were weaned back onto water and accustomed to handling and the experimental environment. Each rat was exposed to a heat stress of 37oC for 2 hours. Peritoneal temperature (Tc) was measured every 2 minutes using a radiotelemeter system. Relative differences in salivation between the groups was determined using the "spit-print" technique. All animals survived the heating protocol and were sacrificed 24 hours later and the extent of the lesion determined. A successful AV3V lesion was defined as ablation of the organum vasculosum of the lamina terminalis and the median preoptic nucleus and variable amounts of damage to the periventricular preoptic and medial preoptic nuclei. **RESULTS:** There was no difference between sham and AV3V Tc at the start of the experiment. AV3V rats Tc rose to significantly higher levels than that of shams during the 2 hour heat stress (41.5oC ± 0.52 vs 38.4oC ± 0.26, $P < 0.01$). AV3V rats also lost significantly less body weight (3.3% ± 0.49 vs 6.3% ± 0.16, $P < 0.01$) and this was reflected in a reduced "saliva positive" area on the spit prints (15.3% ± 3.47 vs 36.8% ± 4.56, $P < 0.05$). **CONCLUSIONS:** These data suggest that salivation is stimulated in response to a heat stress by excitatory inputs mediated through the AV3V region. It is hypothesized that these stimuli may be both humoral (e.g.angiotensin II) and neural (e.g. temperature sensitive neurons in the MnPO) in origin. Supported by a grant from the American College of Sports Medicine Research Foundation.

1258 EFFECT OF AN HERBAL SUPPLEMENT ON THERMOREGULATORY, CARDIOVASCULAR, AND METABOLIC RESPONSES DURING SUBMAXIMAL EXERCISE

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A number of herbal supplements such as Lepidium meyenii, synephrine, guarani and Guarana have been reported to have thermogenic qualities (i.e., have demonstrated an increase metabolic rate) in an effort to increase weight loss. **PURPOSE:** This investigation evaluated the thermoregulatory, cardiovascular, and metabolic responses of an herbal supplement during rest, submaximal exercise and during the post-exercise recovery period. **METHODS:** Five male subjects (25±5 yr) exercised for 30 min (60% of heart rate reserve) on a cycle ergometer at room temperature (24°C). Each subject completed a placebo (PL) trial and a supplement (SUPP) trial that were assigned in a double-blind manner. **RESULTS:** ANOVA with repeated measures across time and condition was used to measure differences in oxygen consumption (VO_2), respiratory exchange ratio (RER), rectal temperature (T_{re}), skin temperatures (T_{sk}) and heart rate (HR). There were no significant differences between PL and SUPP for HR, T_{re}, T_{sk}, VO_2, and RER. However, a main effect for time for these parameters was demonstrated. **CONCLUSION:** These data suggest that the herbal supplement did not demonstrate a differential response in HR, T_{re}, T_{sk}, VO_2, and RER. The lack of significant difference may in part be attributed to the confounding influence of the body weight related dose - response relationship that was not accounted for in the present investigation.

1259 WEARING A CAP, THERMAL BALANCE, AND THERMAL SENSATION DURING RUNNING IN A WARM ENVIRONMENT

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Head cooling during exercise in a warm environment removes 20% of the metabolic heat produced, reducing physiological strain, rectal temperature, sweat rate, and thermal discomfort. Wearing a cap during long distance running races in a warm environment is common. Theoretically, wearing a cap during running in a warm environment may impede body heat loss, increasing body core temperature and thermal discomfort, but this is unclear based upon the scientific literature. **PURPOSE :** To determine if wearing a cap alters thermal balance and thermal sensation during running in a warm environment. **METHODS :** Eight (6 males , 2 females) well-trained runners ran for 1 hour at 67% VO_2max in a warm environment (T_{db} = 31 oC, relative humidity = 41%) wearing (CAP) or not wearing (NOCAP) a white cotton/polyester cap. During both running trials, subjects consumed 2 ml $\cdot kg^{-1}$ of water every 15 minutes. Thermal balance was assessed using continuous monitoring of rectal (T_{rec}) and skin temperatures (T_s , weighted mean : forehead, chest, lower back, forearm, palm, thigh) as well as measurement of whole-body sweat loss and thermal sensation of the head and overall body (10-point scale). **RESULTS :** Mean (± SEM) T_{rec} rose steadily from 36.81 (± 0.24) oC to 38.16 (± 0.15) oC during NOCAP and from 36.76 (± 0.19) oC to 38.27 (± 0.29) oC during CAP. There were no significant differences in T_{rec} or T_s ($p>0.05$) between groups. One hour of running in a warm environment elicited a whole-body sweat loss of 1.23 (± 0.11) liters during NOCAP and 1.30 (± 0.13) liters during CAP with no differences ($p > 0.05$) between treatments. Ratings of thermal sensation for the head and overall body indicated that subjects felt warm during both NOCAP and CAP, with no differences ($p >0.05$) between running trials. Heart rate increased similarly to 164 (± 3.88) and 166 (± 8.38) beats $\cdot min^{-1}$ during the last 5 minutes of NOCAP and CAP. Rating of perceived exertion averaged 12.5 (± 0.73) and 13.38 (± 1.15) during the last few minutes of NOCAP and CAP, respectively, with no differences ($p > 0.05$) between groups. **CONCLUSION :** Wearing a cap during prolonged, moderate intensity running in a warm environment does not signficantly alter thermal balance, thermal sensation, or physiological stress. Therefore, such a practice should not compromise endurance performance or increase the incidence of thermal injury.

1260 PHYSIOLOGICAL RESPONSES IN PROTECTIVE CLOTHING TO TWO HOT ENVIRONMENTS AT EQUIVALENT WBGT LEVELS

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The ability to work for extended periods while wearing encapsulating protective clothing (PC) is often limited by elevated heat storage within the body. The wet-bulb globe temperature (WBGT) is the most often used index used for assessing environmental heat stress. Additionally, the WBGT is used to predict or establish the length of time that work can be performed while wearing PC. However, the WBGT does not reflect the micro-environmental temperature and humidity levels within PC that the worker is experiencing. As a result, WBGT may seriously underestimate the actual heat strain of the worker under varied conditions. **PURPOSE:** To determine the relative influence of dry-bulb and wet-bulb variations, at an equivalent WBGT, on physiological and subjective measures of heat strain during a simulated work protocol while wearing PC. **METHODS:** Five male subjects in a repeated measures design performed two work tests consisting of walk/arm curl combination at a time-weighted work rate of 1.0L/min (300kcal/hr), once at 30oC WBGT. One trial was performed in a hot-wet (HW) condition (Twb=29, Tg=31, Tdb=32), and the other trial in a hot-dry (HD) condition (Twb=23, Tg=47, Tdb=45). **RESULTS:** Significant differences were found between the trials ($p<0.05$) for the HD trial resulting in greater physiological heat strain. Core temperature (Tre), micro-environment temperature (MEt), micro-environment humidity (MEh), sweat rate (SR), sweat evaporation rate (ER), and heart rate (HR) were all greater ($p<0.05$) in the HD with mean skin temperature (Tsk) showing no differences ($p>0.05$) between the two environments. Subjective data of thermal sensation (THERM), perceived exertion (RPE), and a perceptual thermal sensation questionnaire also revealed significantly greater strain while working in HD. **CONCLUSION:** These observation support previous research stating that a 0.5*wet-bulb + 0.5*dry-bulb temperature weightings may be a better predictor for heat strain in PC. Additional research is needed into the validation and existence of a thermally appropriate measure across the range of environmental stress that occurs while working in PC.

F18L FREE COMMUNICATION/POSTER EPIDEMIOLOGY AND PREVENTIVE MEDICINE

1261 RETRIEVAL OF INDIVIDUAL PATIENT DATA FOR AN EXERCISE-RELATED META-ANALYSIS

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PURPOSE: To examine the level of success of acquisition of individual patient data (IPD) for a meta-analysis on the effects of exercise on bone mineral density in adults. **METHODS:** For the purpose of obtaining IPD, studies were selected from a database that contained 76 studies that met our previously defined meta-analytic inclusion criteria. Initial and follow-up request letters for IPD, separated by approximately five weeks, were sent via postal-mail to the appropriate authors of the 76 studies. All authors who provided IPD were sent $40.00 [US] to help cover expenses. **RESULTS:** Of the 76 eligible studies we were able to obtain data from 29 (38.2%). Binary multiple logistic regression analysis revealed a trend suggesting that authors of studies conducted in the United States were less likely to supply IPD when compared with authors who conducted studies in other countries (adjusted odds ratio = 0.324, 95% confidence interval = 0.104 to 1.004). Only 19.0% of authors from studies conducted in the United States versus 52.9% of authors from other countries provided us with IPD. None of the other variables in this model (gender of author, source of publication, year of publication) were significant predictors for whether IPD were provided. **CONCLUSIONS:** The results suggest moderate success in the acquisition of IPD for a meta-analysis dealing with the effects of exercise training on bone mineral density in adults. We were more successful when IPD were requested from studies conducted in countries other than the United States. Given the relatively low response rate, the traditional use of summary data for meta-analysis may be more appropriate for examining the effects of exercise training on bone mineral density in adults.

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Exercise and bone mineral density at the femoral neck in postmenopausal women: A meta-analysis of controlled clinical trials using individual patient data

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The purpose of this study was to conduct a meta-analysis using individual patient data (IPD) in order to examine the efficacy of exercise for improving bone mineral density (BMD) at the femoral neck in postmenopausal women. Ten controlled clinical trials that included 595 subjects ages 42 to 92 years met our criteria for inclusion. Across all designs and categories, there was an increase in BMD of 0.73 +/- 5.52% and 0.45 +/- 6.78% respectively, in the exercise and control subjects. However, comparison of initial and final BMD values between exercise and control subjects revealed no statistically significant effect of exercise on femoral neck BMD. In addition, random-effects analyses revealed no statistically significant within or between-group differences for studies in which IPD were available versus those that were not. In conclusion, the results of this study suggest that exercise is not efficacious for improving and/or maintaining femoral neck BMD in postmenopausal women. However, a need exists for additional research in this area before clinical recommendations can be made regarding the effectiveness of exercise for improving and/or maintaining femoral neck BMD in postmenopausal women.

Learning Objectives: At the end of this session, the participant will be able to

- Describe the current state of knowledge regarding the effects of exercise on bone mineral density at the femoral neck in postmenopausal women.
- Describe the effects of potentially confounding variables on changes in bone mineral density at the femoral neck in postmenopausal women as a result of exercise.
- Describe weaknesses in the literature and identify areas for future research dealing with the effects of exercise on bone mineral density at the femoral neck in postmenopausal women.

Keywords: Exercise, Aging

Presenting author's disclosure statement:

I wish to disclose that I have **NO** financial interests or other relationship with the manufactures of commercial products, suppliers of commercial services or commercial supporters.

Research Issues among Older Adults

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